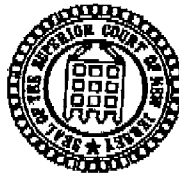


## SUPERIOR COURT OF NEW JERSEY

CHARLES J. WALSH  
JUDGE



BERGEN COUNTY JUSTICE CENTER  
HACKENSACK, NJ 07601-7689  
(201) 327-2690

SUPERIOR COURT BERGEN COUNTY  
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RE: IN RE: DIET DRUG LITIGATION  
Master Docket No. BER-L-13379-04MT

KIM W. BOWLDEN v. WYETH, INC.  
Docket No. BER-L-3026-04MT

KAYELA J. BRADFORD v. WYETH, INC.  
Docket No. BER-L-2432-04MT

KAREN I. BRAILSFORD v. WYETH, INC.  
Docket No. BER-L-3036-04MT

LADAUN G. BRENCHLEY v. WYETH, INC.  
Docket No. BER-L-2407-04MT

SYLVIA BUNKALL v. WYETH, INC.  
Docket No. BER-L-2421-04MT

ROCHELLE CALL v. WYETH, INC.  
Docket No. BER-L-2387-04MT

JAYNE CHATTERTON v. WYETH, INC.  
Docket No. BER-L-2386-04MT

ERMA L. CONOVER v. WYETH, INC.  
Docket No. BER-L-2385-04MT

CAROL G. COULAM v. WYETH, INC.  
Docket No. BER-L-2462-04MT

ROBERT COWGILL v. WYETH, INC.  
Docket No. BER-L-2416-04MT

LISA CREBS v. WYETH, INC.  
Docket No. BER-L-2424-04MT

DELILAH DAVIS v. WYETH, INC.  
Docket No. BER-L-2460-04MT

MARCIA DeWITTE v. WYETH, INC.  
Docket No. BER-L-2475-04

DANIELLE EYRE v. WYETH, INC.  
Docket No. BER-L-2461-04MT

JUDY M. FIELDING v. WYETH, INC.  
Docket No. BER-L-2470-04MT

WALLACE J. HUNSAKER v. WYETH, INC.

Docket No. BER-L-3310-04MT

VICKIE A. HYMAS v. WYETH, INC.

Docket No. BER-L-2354-04MT

SUSAN K. JENSEN v. WYETH, INC.

Docket No. BER-L-2349-04MT

DARLENE JEWKES v. WYETH, INC.

Docket No. BER-L-2345-04MT

WINIFRED LIPPOLD v. WYETH, INC.

Docket No. BER-L-2377-04MT

BEVERLY LLEWELYN v. WYETH, INC.

Docket No. BER-L-2376-04MT

PAULETTE MADSEN v. WYETH, INC.

Docket No. BER-L-3025-04MT

KIM MALDONADO v. WYETH, INC.

Docket No. BER-L-3029-04MT

DIXIE D. MANESS v. WYETH, INC.

Docket No. BER-L-3032-04MT

CAROL MANN v. WYETH, INC.

Docket No. BER-L-3033-04MT

LAURA L. McCOLGAN v. WYETH, INC.

Docket No. BER-L-3039-04MT

VICKIE NIESPOREK v. WYETH, INC.

Docket No. BER-L-2371-04MT

LaVERNE PENA v. WYETH, INC.

Docket No. BER-L-2319-04MT

LEANN PICKETT v. WYETH, INC.

Docket No. BER-L-2369-04MT

ROBIN N. PLATT v. WYETH, INC.

Docket No. BER-L-2317-04MT

DEBORAH POULSON v. WYETH, INC.

Docket No. BER-L-2314-04MT

KAY RAMSEY v. WYETH, INC.

Docket No. BER-L-2313-04MT

CHRISTINE SHAKESPEAR v. WYETH, INC.

Docket No. BER-L-2367-04MT

EVA TUCKER v. WYETH, INC.

Docket No. BER-L-2357-04MT

APPLICATIONS CHALLENGING ELIGIBILITY TO EXERCISE OPT-OUTS  
FROM NATIONWIDE CLASS ACTION SETTLEMENT

MOVANT: WYETH CORPORATION

MOVANT'S ATTORNEYS: PORZIO, BROMBERG & NEWMAN (ANITA HOTCHKISS, ESQ., APPEARING), ARNOLD & PORTER (ANAND AGNESHWAR, ESQ. AND CARA PETERSEN, ESQ., APPEARING), REED SMITH LLP (DANIEL K. WINTERS, ESQ., APPEARING), MITCHELL, McNUTT & SAMS (JOHN G. WHEELER, ESQ., APPEARING), GHOLSON & ORR (ROBERT D. GHOLSON, ESQ., APPEARING), HERTEN, BURSTEIN, SHERIDAN, CEVASCO, BOTTINELLI, LITT, TOSKOS & HARZ (THOMAS J. HERTEN, ESQ., APPEARING), RAMSAY & HAMMOND (J. ROBERT RAMSAY, ESQ., APPEARING).

OPPONENTS: MONYA A. ADAMSON, KIMBERLY M. ALTHAUSEN, JUDY ALVEY, GWENDOLYN ANDERSON, MARIANNE ANDERSON, SHERYL A. ANDERSON, TERILYN ANDERSON, LANECE ANDREASON, LAURA AYEN, PAMELA BEDDOES, LAURIE BENSON, LYNETTE BINGHAM, DEBORAH BOOTS, KIM W. BOWLDEN, KAYELA J. BRADFORD, KAREN I. BRAILSFORD, LADAUN G. BRENCHLEY, SYLVIA BUNKALL, ROCHELLE CALL, JAYNE CHATTERTON, ERMA L. CONOVER, CAROL G. COULAM, ROBERT COWGILL, LISA CREBS, DELILAH DAVIS, MARCIA DEWITTE, DANIELLE EYRE, JUDY M. FIELDING, WALLACE J. HUNSAKER, VICKIE A. HYMAS, SUSAN K. JENSEN, DARLENE JEWKES, WIFRED LIPPOLD, BEVERLY LLEWELYN, PAULETTE MADSEN, KIM MALDONADO, DIXIE D. MANESS, CAROL MANN, LAURA L. MCCOLGAN, VICKIE NIESPOREK, LAVERNE PENA, LEANN PICKETT, ROBIN N. PLATT, DEBORAH POULSON, KAY RAMSEY, CHRISTIEN SHAKESPEAR, AND EVA TUCKER.

OPPONENTS' ATTORNEYS: WILLIAMS BAILEY LAW FIRM (E. ARMISTEAD EASTERBY, ESQ., AVRAM J. BLAIR, ESQ., AND AMY M. CARTER, ESQ., APPEARING).

HEARINGS: YES

LETTER OPINION: MAY 6, 2005 (AMENDED AS BELOW MAY 9, 2005)

This matter is before the Court on applications by Wyeth Corporation, as the successor to American Home Products Corporation ("AHP") and each of its former subsidiaries, affiliates and divisions (collectively "Wyeth" or "defendants") challenging the eligibility of forty-seven (47) plaintiffs to exercise opt-outs from the Nationwide Class Action Settlement ("CAS"). These plaintiffs are: Monya A. Adamson ("Adamson"); Kimberly M. Althausen ("Althausen"); Judy Alvey ("Alvey"); Gwendolyn Anderson ("G. Anderson"); Marianne Anderson ("M. Anderson"); Sheryl A. Anderson ("S. Anderson"); Terilyn Anderson ("T. Anderson"); LaNece Andreason ("Andreason"); Laura Ayen ("Ayen"); Pamela Beddoes ("Beddoes"); Laurie Benson ("Benson"); Lynette Bingham ("Bingham"); Deborah Boots ("Boots"); Kim W. Bowlden ("Bowlden"); Kayela J. Bradford ("Bradford"); Karen I. Brailsford ("Brailsford"); Ladaun G. Brenchley ("Brenchley"); Sylvia Bunkall ("Bunkall"); Rochelle Call ("Call"); Jayne Chatterton ("Chatterton"); Erma L. Conover ("Conover"); Carol G. Coulam ("Coulam"); Robert Cowgill ("Cowgill"); Lisa Crebs ("Crebs"); Delilah Davis ("Davis"); Marcia DeWitte ("DeWitte"); Danielle Eyre ("Eyre"); Judy M. Fielding ("Fielding"); Wallace J. Hunsaker ("Hunsaker"); Vickie A. Hymas ("Hymas"); Susan K. Jensen ("Jensen"); Darlene Jewkes ("Jewkes"); Wifred Lippold ("Lippold"); Beverly Llewelyn ("Llewelyn"); Paulette Madsen ("Madsen"); Kim Maldonado ("Maldonado"); Dixie D. Maness ("Maness"); Carol Mann ("Mann"); Laura L. McColgan ("McColgan"); Vickie Niesporek ("Niesporek"); LaVerne Pena ("Pena"); Leann Pickett ("Pickett"); Robin N. Platt ("Platt"); Deborah Poulson ("Poulson"); Kay Ramsey ("Ramsey"); Christien Shakespear ("Shakespear"); and Eva Tucker ("Tucker").

The Court conducted its fifth evidentiary hearing on Wyeth's challenges which began on April 11, 2005 and concluded on April 30, 2005. During that period, the Court heard testimony given by: Martin E. Goldman, M.D. ("Dr. Goldman"); Charles Gibbs Vasey, M.D. ("Dr. Vasey"); Muhamed Saric, M.D. PhD ("Dr. Saric"); Mark V. Sherrid, M.D. ("Dr. Sherrid"); Arthur Millman, M.D. ("Dr. Millman"); Chunguang Chen, M.D. ("Dr. Chen"); Aasha S. Gopal, M.D. ("Dr. Gopal"); Kenneth Ong, M.D. ("Dr. Ong"); Jeffrey G. Schwartz, M.D. ("Dr.

Schwartz”); Paul Michael Wangenheim, M.D. (“Dr. Wangenheim”); Michael S. Mancina, M.D. (“Dr. Mancina”); and Eric H. Stern, M.D. (“Dr. Stern”); all of whom were cardiologists. The Court also heard the testimony of James D. Thomas, M.D. (“Dr. Thomas”), a cardiologist with expertise in the field of applied mathematics and physics and Frank Miele (“Miele”), an engineer and physicist. Much of the direct testimony of each of these witnesses was presented through affidavits, certifications or reports which were adopted during the course of the evidentiary hearing. In addition, the Court considered the contents of several treatises which were recognized in the proceedings as reliable under **N.J.R. EVID. 803(c)(18)**, including: Harvey Feigenbaum, **ECHOCARDIOGRAPHY** (5<sup>th</sup> Ed. 1994) (“Feigenbaum 5<sup>th</sup> Edition Text”); Harvey Feigenbaum, **ECHOCARDIOGRAPHY** (6<sup>th</sup> Ed. 2004) (“Feigenbaum 6<sup>th</sup> Edition Text”); Arthur Weyman, **PRINCIPLES AND PRACTICES OF ECHOCARDIOGRAPHY** (2<sup>nd</sup> Ed. 1994) (“Weyman Text”); Novin C. Nanda, **ATLAS OF COLOR DOPPLER ECHOCARDIOGRAPHY** (1989); J.P. Singh, et al., *Prevalence and Clinical Determinants of Mitral, Tricuspid, and Aortic Regurgitation (The Framingham Heart Study)*, *Am. J. Cardiology*: 83 (1999) (“Singh”); Miguel A. Quiñones, M.D., et al., *Recommendations for Quantification of Doppler Echocardiography: A Report From the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography*, *American Society Of Echocardiography Report*, *J. Am. Soc. Echocardiogr.* (2002); James D. Thomas, M.D., et al., *Quantification of Jet Flow by Momentum Analysis An In Vitro Color Doppler Flow Study*, *Circulation*: 81, 248 (1990); J. Geoffrey Stevenson, M.D., *Two-Dimensional Color Doppler Estimation of the Severity of Atrioventricular Valve Regurgitation: Important Effects of Instrument Gain Setting, Pulse Repetition Frequency, and Carrier Frequency*, *J. Am. Soc. Echocardiography* 2: 1-10 (1989); and *The Task Force on Valvular Regurgitation Recommendation for Evaluation of the Severity of Native Valvular Regurgitation with Two-dimensional and Doppler Echocardiography (“ASE Standards”)*, *J. Am. Soc. Echocardiography*, 16: 777 (2003).

The Court previously discussed the standards to be used in assessing these eligibility challenges. *In Re: Diet Drug Litigation*, BER-L-7718-03 (Law Division April 13, 2004) (“*Eligibility Standards Opinion*”) (slip op. at 31-36). Each plaintiff seeking to exercise an intermediate opt-out (“IOO”) or back end opt-out (“BEOO”) is required by the CAS to establish that he or she is FDA Positive by a qualifying echocardiogram. FDA Positive, as defined, contains two (2) standards. First, the quantitative measurements that constitute FDA Positive heart valve regurgitation are as follows:

Aortic Valve – Mild or greater regurgitation, defined as regurgitant jet diameter in the parasternal long-axis view (or in the apical long-axis view, if the parasternal long-axis view is unavailable), equal to or greater than ten percent (10%) of the outflow tract diameter (JH/LVOT).

Mitral Valve – Moderate or greater regurgitation, defined as regurgitant jet area in any apical view equal to or greater than twenty percent (20%) of the left atrial area (RJA/LAA).

CAS § I.22.b. The CAS also requires that specific criteria be used in determining whether these levels of valvular regurgitation are present. Singh at 897-98.

Second, the CAS requires the echocardiograms be performed and evaluated by “qualified medical personnel” in accordance with the methodology set forth in two (2) referenced texts – the Feigenbaum 5<sup>th</sup> Edition Text and the Weyman Text. *Eligibility Standards Opinion* (slip op. at 12-16).

This Court already has determined that “Wyeth [may] disqualify an IOO or BEOO if it establishes that the performance and/or evaluation of the echocardiogram (at issue) was medically unreasonable as a matter of law. Stated another way, Wyeth “[may] . . . disqualify . . . [an] IOO or BEOO if it can show that . . . [an] expert’s conclusions respecting the echocardiogram supporting the opt-out could not ‘reliably flow from the facts known to the expert and the methodology used.’” *Eligibility Standards Opinion* (slip op. at 31) (citations omitted).

For the reasons which follow, the Court finds that Wyeth has satisfied the Court that the echocardiograms supporting claims of plaintiffs: Kimberly M. Althausen, Judy Alvey, Gwendolyn Anderson, Marianne Anderson, Sheryl A. Anderson, LaNece Andreason, Laura Ayen, Pamela Beddoes, Laurie Benson, Lynette Bingham, Deborah Boots, Kayela J. Bradford, Karen I. Brailsford, Ladaun G. Brenchley, Sylvia Bunkall, Rochelle Call, Jayne Chatterton, Erma L. Conover, Carol G. Coulam, Robert Cowgill, Lisa Crebs, Danielle Eyre, Judy M. Fielding, Wallace J. Hunsaker, Vickie A. Hymas, Susan K. Jensen, Darlene Jewkes, Winifred Lippold, Beverly Llewelyn, Paulette Madsen, Kim Maldonado, Dixie D. Maness, Carol Mann, Laura L. McColgan, Vickie Niesporek, Robin N. Platt, Deborah Poulson, Kay Ramsey, Christine Shakespear, and Eva Tucker have not

been performed and/or interpreted in a medically reasonable manner. Accordingly, the Complaints filed by these plaintiffs are dismissed and those plaintiffs are returned to the Class. The Court, however, finds that Wyeth has failed to support its eligibility challenge as to plaintiffs: Monya A. Adamson, Terilyn Anderson, Kim W. Bowlden, Delilah Davis, Marcia DeWitte, LaVerne Pena, and Leann Pickett. Accordingly, Wyeth's motion to dismiss will be denied as to them. The findings of fact and conclusions of law supporting these determinations are reported below.

## I

### A.

In order to determine whether Wyeth's challenges have merit, one has to understand the underlying medical conditions claimed by these plaintiffs and the tools used to detect and treat those conditions. Mild aortic and moderate mitral regurgitation are the two (2) medical conditions that permit either an IOO or BEOO. These conditions involve the backward or reverse flow of blood through defective valves during the heart's pumping cycle.

The heart consists of four (4) chambers: the right atrium, the right ventricle, the left atrium and the left ventricle. The right atrium receives deoxygenated blood from the body and ejects that blood into the right ventricle through the tricuspid valve; the right ventricle then pumps that blood across the lungs through the pulmonic or pulmonary valve for oxygenation. The oxygenated blood, in turn, is received by the left atrium, which ejects blood into the left ventricle through the mitral valve. The left ventricle then pumps that oxygenated blood into the aorta through the aortic valve, and from there to the rest of the body. The heart chambers are connected by valves that open to allow blood to pass through and then close to prevent significant backflow. This process ensures the proper directional flow of blood through the heart.

The chambers of the heart fill and empty in a two-phase cardiac cycle that comprises diastole - - the filling cycle, and systole - - the emptying cycle. For our purposes, we are concerned with the active contraction of the left ventricle and pumping of blood into the aorta through the open aortic valve during systole. Throughout this phase the mitral valve is closed to prevent backward flow or regurgitation from the left ventricle into the left atrium. We are also interested in the other phase of the cardiac cycle -- diastole -- which occurs when blood enters the left ventricle through the open mitral valve. During this phase the aortic valve

is closed to prevent leakage or regurgitation from the aorta back into the left ventricle.

Healthy heart valves rarely prevent all regurgitation. When these valves are closed there may be a minimal amount of leakage -- trace regurgitation. Moreover, during routine valve closure, blood caught between the valve leaflets is displaced backward resulting in some blood backflow. This backward displacement of blood is considered part of the closing process, and is not regurgitation. According to Weyman, “true” mitral regurgitation “should last throughout most or all of systole.” Weyman Text at 429. A brief or non-sustained jet of mitral regurgitation is an indication that the regurgitation is usually less than mild. The same source teaches that “true” aortic regurgitation should continue “throughout diastole.” *Id.* at 529. Aortic regurgitation that is brief or non-sustained is usually less than mild.

Normally blood flows at a uniform velocity in a forward direction. This normal blood flow is laminar. Regurgitant flow, on the other hand, produces a jet of mixed velocities which is turbulent. It is this turbulent flow which is one of the focuses of echocardiography.

According to Singh, the degree of valvular regurgitation or valvular insufficiency is classified as trace, mild, moderate, or severe. Trace aortic regurgitation and trace and mild mitral regurgitation are common in the general population and are considered normal findings. Singh at 900.

## **B.**

Echocardiography is a principal technique used to evaluate the heart, including its function, structure and the flow of blood through it. The underlying principle involved in echocardiography is the use of high frequency sound waves. A transducer is placed on the patient’s chest wall which emits sound waves that bounce off of the heart’s structures, and that information is translated into moving images of those structures on a screen. There are several different techniques available in echocardiography. The technique relevant here is Doppler echocardiography. “Doppler echocardiography is based on the change in frequency of a sound wave that occurs when it strikes a moving target – in this case the red blood cells.” Weyman Text at 143.

Color flow Doppler is used to display the movement of blood flow through the heart by assigning different colors depending upon the direction and velocity of the blood flow. By convention, laminar blood flowing towards the transducer is

depicted in shades of red, and laminar blood flowing away from the transducer is depicted in shades of blue; darker shades indicating slower velocity and lighter shades higher velocity. *See* Feigenbaum 5<sup>th</sup> Edition Text at 33. Turbulent blood flow is depicted in a “mosaic,” multi-colored pattern, thus displaying the different velocities and directions of the blood in the area under study. The absence of blood flow is depicted by black on color flow Doppler. Thus, in Doppler echocardiography blood flow is represented as discrete color areas (jets) in real time, superimposed on two-dimensional images of the heart’s structure.

The quality of an echocardiogram depends on a number of factors including: the patient’s body; the technical skill of the physician or sonographer performing the study; the equipment used and its settings; and, the physician’s interpretation and measurements. The proper performance of an echocardiogram in the cases before this Court must follow the guidelines set forth in the Weyman and Feigenbaum 5<sup>th</sup> Edition Texts.

Settings on the echocardiographic equipment can have a substantial impact on the quality of the images and the accuracy of the recordings. Two (2) key settings on the equipment are referred to as the Nyquist limit and gain setting. The Nyquist limit establishes the maximum velocity of laminar blood flow that can be detected in a monochromatic fashion (solid color).<sup>1</sup> When the velocity of the blood flow exceeds the pre-set Nyquist limit the color depicting the blood flow “wraps around” so that if the flow is laminar it appears to be flowing in the opposite direction. Turbulent blood flow in such circumstances appears as a “mosaic,” multi-colored pattern. If the Nyquist limit is set too low, the velocity of normal blood flow may exceed a low Nyquist setting and will appear as turbulent regurgitation, even though it is actually normal non-regurgitant flow. Additionally, when the Nyquist limit is set too low it will exaggerate the degree of any regurgitation present by including normal blood flow velocity in the turbulent regurgitant jet area. Virtually all the experts who testified here agree that a higher Nyquist limit generally leads to a more reliable echocardiogram. A recent

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<sup>1</sup> As the Feigenbaum 5<sup>th</sup> Edition Text at 29 notes:

The major disadvantages of pulsed Doppler is that the velocity one can measure is limited. The pulsed system inherently has a pulsed repetition frequency or PRF. The PRF determines how high a Doppler frequency the pulse system can detect.... The inability of a pulsed Doppler system to detect high-frequency Doppler shifts is known as “aliasing.” The upper limit of frequency that can be detected with a given pulsed system is known as the “Nyquist” limit or number. This limit is defined as one half the pulse repetition frequency or PRF.

*See* Miele Certification at ¶¶ 16, 17, 31 and 32.

consensus report by the American Society of Echocardiography stressed the importance of an appropriate Nyquist limit.

Numerous technical, physiologic and anatomic factors affect the size of the regurgitant area and therefore alter its accuracy as an index of regurgitation severity. Jet size is affected by instrument factors, especially pulse repetition frequency (PRF) and color gain. Standard technique is to use a Nyquist limit (aliasing velocity) of 50/60 cm/sec, and a color gain that just eliminates random color speckle from non-moving regions. Jet area is inversely proportional to PRF, and *substantial error can be introduced with use of higher or lower settings* than the nominal settings to which echocardiographers have become accustomed.

*ASE Standards* at 777-778 (emphasis added).

A color Doppler gain setting is another important variable in the echocardiographic system. If the gain on echocardiographic equipment is set too high, the image may be artificially increased and may also present “background noise” or “speckling,” seriously degrading the quality of the echocardiogram and making it difficult to assess true regurgitation. Weyman Text at 240-241 and 258. As Weyman teaches, the “detection of the Doppler frequency shift is critically dependent on the signal/noise ratio, and every effort must be made to maximize this relationship.” Weyman Text at 256. To do so, Weyman suggests that:

Ideally, as in imaging studies, one begins with a high gain setting to be sure that all of the signal present is appreciated. The gain is then gradually decreased to a point where the signal is optimally displayed and the associated noise and mirroring artifacts ... are at a minimum.

Weyman Text at 258.

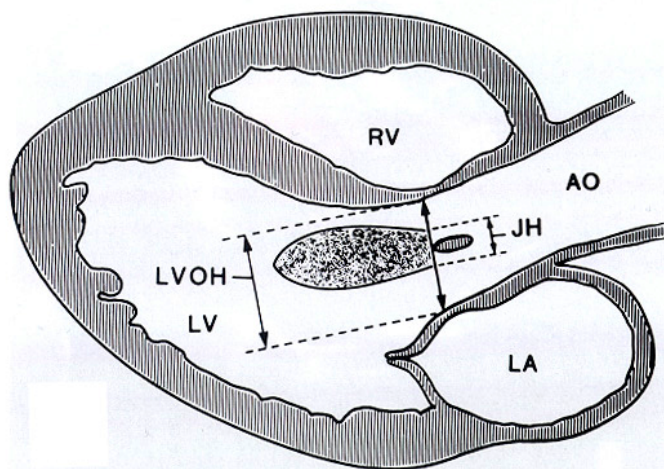
Two (2) dimensional or 2-D gain settings are also significant. The 2-D gain is important in acquiring and displaying cardiac structures such as the left atrium and ventricle. If the 2-D gain is set too high, these cardiac structures are obscured as the display takes on an appearance of a snow storm. Obviously, this can be

quite significant when one must trace the left atrial area in making the area measurements required by the CAS.

Another important technical aspect of echocardiographic acquisition relates to the angle the transducer is placed relative to the heart when images are recorded. If those images are not acquired in the appropriate angle or plane, the amount of regurgitation and the sizes of the chambers of the heart may appear larger or smaller than they really are. Again, Weyman teaches that “[D]oppler frequency shifts are maximal when the sound beam is parallel to the flow vector (*i.e.*, aligned parallel to the path of blood flow in the vessel of interest)... The Doppler beam, therefore, is ideally aligned parallel, rather than perpendicular, to flow because larger frequency shifts are easier to detect and the output is less subject to random fluctuation.” Weyman Text at 256.

FDA Positive heart valve regurgitation involving the aortic valve requires that two (2) measurements be made: (1) the height of the jet of aortic regurgitation (“JH”); and (2) the height of the left ventricular outflow tract (“LVOT”).<sup>2</sup> The JH measurement is the linear width of the jet of aortic regurgitation as it leaks backward into the left ventricle. Feigenbaum tells us that this measurement must be made as close as possible to the point of origin of that jet on the ventricular side of the aortic valve. Feigenbaum 5<sup>th</sup> Edition Text at 283. Otherwise, the

<sup>2</sup> The same diagram illustrating how this measurement is actually made is displayed in the Feigenbaum 5<sup>th</sup> Edition Text at 285, Fig. 6-101, and the Weyman Text at 534. The illustration as it appears in Weyman is reproduced below.



**Fig. 19-61.** The measurement of regurgitant jet height. Regurgitant jet height (JH) is measured at the aortic valve level in the parasternal long axis view. AO = aorta; LA = left atrium; LV = left ventricle; LVOH = left ventricular outflow tract height; RV = right ventricle. (From Perry GJ, et al.; Evaluation of aortic insufficiency by Doppler color flow mapping. J Am Coll Cardiol 9:952, 1987. Reprinted with permission from the American College of Cardiology.

measurement will be exaggerated by the spray or “nozzle effect” that occurs when high velocity liquid (regurgitant blood) is ejected through a narrow orifice into a lower pressure chamber (the left ventricle in diastole). *Id.* at 283. The LVOT is the region of the left ventricle below the aortic valve. These two (2) measurements are then expressed as a ratio, JH/LVOT. Current technology utilizes digitally calibrated calipers or cursors, which can measure the linear width of the JH and LVOT on a frozen frame or image using a digitally calibrated caliper or cursor, from commercially available software packages.

The definition of FDA Positive mitral regurgitation also requires two (2) measurements to be made: (1) the regurgitant jet area, or “RJA”; and (2) the left atrial area, or “LAA.” Unlike the linear width measurements made of the JH and LVOT, the RJA and LAA are area measurements. Again these measurements are expressed as a ratio, RJA/LAA, in assessing the degree of mitral regurgitation. These measurements of the RJA and LAA can be done while the sonographer is acquiring the study, or off-line, and are referred to as tracings or planimetry when using the technology just described.

## II

### A.

The Court considered the qualifications of the experts as required by **N.J.R. EVID. 702**. *Kemp ex rel Wright v. State*, 174 N.J. 412, 427 (2002). Overall, the Court found the experts called by Wyeth and the plaintiffs to be well qualified, or at least qualified, in the areas offered.

The Court finds Drs. Goldman, Chen, Vasey, Schwartz, Wangenheim, Stern and Thomas well qualified in the field of echocardiography. Dr. Thomas is also an expert on the theory of echocardiography and its mathematical expression. Dr. Goldman is a Professor of Medicine at the Mt. Sinai School of Medicine in New York and has taught at that medical school for over twenty (20) years. Dr. Goldman has written extensively in the field of echocardiology, holds positions as a director of the American Society of Echocardiography (“ASE”), one of the bodies seeking to promote advances in the field of echocardiography, and serves on several of its committees. He is the immediate past President of the New York Echocardiography Society. Dr. Chen is a Clinical Professor of Medicine at the Mt. Sinai School of Medicine in New York and is the Director of Cardiac Non-Invasive Laboratory at the Newark Beth Israel Medical Center. He has published extensively in the field of echocardiography and is a Level III echocardiographer.

Dr. Vasey is the Director of Noninvasive Services of Asheville Cardiology Associates, P.A. in Asheville, North Carolina. He is a Clinical Professor of Medicine at the North Carolina School of Medicine. He reads several thousand echocardiograms in his practice and is a Fellow of the ASE. He presently serves on the board of the ASE, as well as its operating committees. Dr. Schwartz currently serves as Director of the Echocardiography Laboratory of Morristown Cardiology Associates. He is board certified in internal medicine, cardiovascular medicine, echocardiography, and nuclear cardiology. He is both a practicing cardiologist and designated teaching service attending at Morristown Memorial Hospital. Dr. Wangenheim is the Medical Director of the Echocardiography Laboratory at the St. Barnabas Medical Center in Livingston, New Jersey and has held that position for the last four (4) years. In this capacity, Dr. Wangenheim reads approximately 3,000 echocardiograms per year. Dr. Stern is an Associate Professor of Medicine at the Mount Sinai School of Medicine in New York City and is Co-Director of the Echocardiography Laboratory at the Mount Sinai Hospital. Dr. Stern also served as Chief of the Echocardiography Laboratory at the Bronx VA Medical Center between 1984 and 1998. Dr. Thomas is presently the Section Head for Imaging within the Department of Cardiovascular Medicine at the Cleveland Clinic Foundation. Dr. Thomas also is a Professor of Medicine and Biomechanical Engineering at the Ohio State University and an Adjunct Professor of Medicine and Biomechanical Engineering at Case Western Reserve. Dr. Thomas also is the Head Scientist for Ultrasound at the National Aeronautics and Space Administration ("NASA") and has advised that agency on the use of ultrasound in manned space flight. He graduated from Harvard University *summa cum laude* in applied mathematics and physics and from Harvard Medical School. He authored Chapter 12 in the Weyman Text entitled "Fluid Dynamics of Regurgitant Jets and Their Imaging by Color Doppler" and has written well over 700 articles in the fields of Cardiology and Echocardiography, among others. Copies of the curricula vitae of these seven (7) physicians are part of the hearing record.

The plaintiffs, too, produced qualified witnesses. Dr. Mancina presently is in private practice in Leavenworth, Kansas with professional licenses in Kansas, Missouri and Indiana. He is a board certified physician holding boards in internal medicine and cardiology with Level II training in echocardiography and interprets 3,500 echocardiograms per year. Dr. Mancina did his fellowship in Cardiology at Indiana University where he studied under Dr. Harvey Feigenbaum. Miele is an engineer with training in physics and echocardiographic machine design. Miele helped design echocardiographic equipment while at Hewlett Packard Corporation and presently has his own consulting business. He teaches physicians and

technicians how to use echocardiographic equipment. The curricula vitae of these experts also are included as part of the record.

The expert cardiologists appointed by the Court under the terms of the *Eligibility Standards Opinion* also are well qualified. Dr. Saric is presently the Director of the Echocardiography Laboratory at the University of Medicine and Dentistry of New Jersey and has Level III echocardiographic training. In addition to his M.D. degree and board certifications in cardiology and echocardiography, Dr. Saric holds a PhD in medical sciences from New York University. Dr. Sherrid is presently the Director of the Echocardiography Laboratory at St. Luke's Roosevelt Hospital Center and serves as an Associate Professor of Clinical Medicine at the Columbia University College of Physicians and Surgeons. He is the President of the New York Echocardiography Society. Dr. Gopal is the Director of Echocardiography at St. Francis Hospital, Roslyn, New York and is an Associate Professor of Medicine at SUNY (Stonybrook, New York). She is a Level III echocardiographer and has published in the field of echocardiography. Dr. Ong is the Acting Chief of Cardiology and the Director of the Cardiac Non-Invasive Imaging Laboratory at the Brooklyn Hospital Center. He is a Level III echocardiographer and has published in the field of echocardiography. Dr. Millman is the Chief of Cardiology at Trinitas Hospital in Elizabeth, New Jersey. He has had extensive experience in echocardiography and teaches cardiology fellows from the Seton Hall Graduate School of Medical Education. The curricula vitae of these experts also are part of the record.

## **B.**

As in the past, the Court's decisions in these individual eligibility cases are based largely on the quality of the echocardiograms. The initial reports of physicians with respect to virtually all these challenged echocardiograms have significantly overstated the pathology observed and/or claimed that the echocardiograms were of good diagnostic quality when they clearly were not. Accordingly, as in the eligibility hearings on the Group 1, Group 2, Group 3 and Group 4 plaintiffs (see *Armstrong et al v. Wyeth, Inc.*, (BER-L-7024-03MT); *Comparato v. Wyeth, Inc., et al* (BER-L-332-04); *Andrade v. Wyeth, Inc.*, (BER-L-1502-04MT); *Adeyemo v. Wyeth, Inc.* (BER-L-1396-04MT) (Letter Opinions dated August 4, 2004, slip op. at 10-12; dated September 22, 2004, slip op. at 14-15; dated December 9, 2004, slip op. at 16-18; and dated February 24, 2005, slip op. at 18-24), the plaintiffs' experts spent much of their time seeking to excuse and explain these overstatements and/or the poor technical quality of the echocardiograms.

In addition, despite significant experience with the hearings, plaintiffs' counsel provided virtually no quantitative information by way of affidavit at the outset but instead attempted to spring the information on Wyeth's counsel at the hearing. While the Court is satisfied that Wyeth ultimately received sufficient information to proceed with the hearings, the Court is convinced that this failure to initially provide plainly relevant information was intentional.

For example, Dr. Mancina's initial affidavit which purported to support opt-outs for all forty-seven (47) plaintiffs was so bereft of information that the Court had to adjourn the hearings so that he could identify the location on the media where his readings of RJA, LAA, JH and LVOT were made. Even the actual JH and LVOT or RJA and LAA measurements were absent from his original affidavit. Instead, only percentage (relative) information was provided. Moreover, Dr. Mancina attempted to expand his affidavit during his first appearance. Despite Dr. Mancina's failure to provide this information, the Court permitted some expansion of his testimony on the subject of Nyquist limits, gain settings and other technical aspects of echocardiography. Dr. Mancina's testimony ended abruptly when he had a diabetic incident prior to his resuming the witness stand on April 12, 2005.<sup>3</sup> Dr. Mancina went home to Leavenworth, Kansas.

The measurements and their location on the echocardiographic media ultimately were provided to Wyeth and the Court electronically on April 18, 2005. In many instances, Dr. Mancina's measurements were made in different locations on the media requiring Wyeth to respond on the fly and limiting the usefulness of the reply certifications and affidavits. When the underlying measurements were finally provided in compliance with this Court's Order, Dr. Mancina again attempted to use that occasion to supplement his testimony on general issues raised in the eligibility challenge proceeding. For example, he claimed to have done a study on the Cypress echocardiogram machine, the equipment used in the overwhelming number of echocardiograms here, which would demonstrate that lower Nyquist settings -- in the 40 cm/sec to 50 cm/sec range -- would not have a tendency to exaggerate the jet height or area. None of this information was provided to Wyeth as was required. Dr. Mancina resumed the witness stand on April 25, 2005. The Court limited his general testimony to that given on April 11, 2005, and declined to permit testimony on this so-called study.

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<sup>3</sup> The Court was advised of Dr. Mancina's health problem on the morning of April 12, 2005.

Miele provided an affidavit for these hearings and was permitted to rely upon a prior affidavit submitted during the Group 1 hearings. Nevertheless, his testimony at the hearing had practically nothing to do with these written submissions. Instead, the questioning was directed to attacking Dr. Thomas' affidavit and Dr. Thomas' testimony on Nyquist settings. While Dr. Thomas' points were made on rebuttal and Miele could not have specifically addressed them in his affidavit, no effort was made to seek this Court's approval for the filing of an additional affidavit or certification. Moreover, it was clear that Miele's initial submission would provoke a response as to the physics surrounding Nyquist settings. Suffice it to say, Miele's testimony dealt with arcane points respecting the physics of echocardiography and fluid dynamics. Wyeth's counsel could not have meaningfully prepared for cross-examination on these points given Miele's prior two (2) written submissions. In addition, plaintiffs' counsel sought to introduce the results of a purported study Miele did on the physical characteristics of the particular echocardiographic machine (the Cypress) used in creating most of these echocardiograms. No notice that the witness had conducted this study, let alone any of its purported results, was ever given to Wyeth's counsel. Accordingly, the Court declined to permit Miele to testify about the study and its supposed conclusions.

As noted, the technical deficiencies in the echocardiograms dominated this hearing. In many instances here, as in the past, color Doppler gain settings were set so high that the entire color box was filled with artifact. If valvular regurgitation was present, it could rarely be identified and could never be reliably quantified. In spite of these defects, Dr. Mancina continually excused the gain settings by saying that either the color speckling was not evident or, if it was, it did not affect his conclusions. But it turns out that Dr. Mancina supervised the performance of approximately 20,000 echocardiograms in connection with efforts to opt-out of the CAS and for other purposes in the phen-fen litigation. In providing guidance to the echocardiographic sonographers working on this project, Dr. Mancina specifically addressed proper gain settings. In two (2) memoranda written in 2002 and 2003, he reminded the sonographers on the phen-fen project that they "[a]lways [should] use gains in the range of 6-11 for color gain" on the Cypress echocardiographic machine. (Emphasis added.) He further cautioned: "Be sure your color gains are not set too high (go up to the point where the color gain causes a spark in the soft tissue and then decrease it so there is no soft tissue color)." However, review of the echocardiograms germane to the proceedings indicate that of the forty-three (43) echocardiograms conducted on the Cypress, thirty-three (33), an astounding seventy-eight percent (78%), had gain settings outside the ranges Dr. Mancina had mandated in his memoranda.

In other instances, Nyquist limits of 41 cm/sec, well below the Nyquist limits outlined in the *ASE Standards* at 777-778 (50-60 cm/sec) and in the Weyman Text at 245 (60-90 cm/sec), appeared in echocardiograms supporting the opt-outs. The low Nyquist settings sometimes appeared in conjunction with high color gain settings, further compounding the problem. In the face of such obvious deviations from proper echocardiographic practice, Dr. Mancina and Miele were left to opine that the capacity of this low Nyquist limit to inflate any observed regurgitant jet was significantly overestimated by Wyeth's and the Court's appointed experts or were overwhelmed by angle effects where views were taken in the PLAX view.<sup>4</sup> It was also claimed that some of the echocardiograms here

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<sup>4</sup> Dr. Mancina testified that Nyquist limits in the 40 cm/sec range were regularly used by sonographers in color Doppler echocardiography.

THE WITNESS: You're going to get the long answer first because there's no short answer to that.

JUDGE WALSH: All right.

THE WITNESS: We looked at the Nyquist for this machine in our hands in our office, looking at valve regurgitation. Because that's what we should do. It's only legitimate and logical and also expected of a person to do that in their own laboratory.

And what we found is that within the ranges that we use daily for looking at valvular regurgitation, which includes 70, 60, 50 and upper 40s, we found no significant difference in the jet size.

\* \* \* \*

JUDGE WALSH: I got that picture.

Let me ask you one other thing: What about the low 40s?

THE WITNESS: Well, I could make a statement that would take a long time to explain.

JUDGE WALSH: We have all the next two days.

THE WITNESS: Okay. It is my opinion that the low 40s makes no difference in the jet size, no clinically significant difference in the jet size. And, yet, it makes it harder to read. In other words, less pleasing to my eye to be at 40 versus 60.

And that's not only my opinion, but that's the opinion of my sonographers, because we discuss that type of topic. So we don't want to be at 40 if we can avoid it. But, you know, some people are really huge people. We do 400-pound people. And there's a depth setting that -- the Nyquist is -- as you know, by the physics of Nyquist, you cannot use 50 or 60 for a person that has a bid AP diameter. So we are left with doing what we have to do, which is quite adequate and it doesn't change --

JUDGE WALSH: Well, it depends on the frequency of the transducer.

THE WITNESS: That's correct. And the filters. I mean, there are a variety of -

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JUDGE WALSH: And the filters.

MR. BLAIR: We're going to talk more about Nyquist in a minute, but I do want to capture that last opinion.

BY MR. BLAIR:

Q. Doctor, is it your opinion that reducing Nyquist on the Cypress machine, in particular, based upon your experience from, say, 50 to the end of the low 40s, does that materially affect regurgitant jet size?

were “technically difficult” because, in some instances, obese plaintiffs required greater probe depths thus lowering the Nyquist. But as will be seen later in this Letter Opinion, these unacceptable Nyquists resulted from the technicians failing to properly adjust the Nyquist limit upward as examinations were conducted. As it turns out, unlike most echocardiographic machines, the Cypress did not automatically adjust the Nyquist limit upward when returning from lower probe depths. Dr. Mancina put it this way:

THE WITNESS: [The Cypress machine] ... does have limitations. I can name them, if you like[.] [I]t has limitations, as all machines do.

JUDGE WALSH: I would like you to name them.

THE WITNESS: Okay. We find that it doesn’t have high PRF and that can limit the pulse Doppler frequencies that you can obtain. It has some features that we have to train our sonographers to deal with, which is *it registers a Nyquist limit and doesn’t change automatically from patient to patient; even from one moment in the study to the next moment. So sonographers have to be trained and have to be attentive to the Nyquist limit that is being used*, because that’s an important consideration in doing ultrasound.

*And, so, if there is not an automatic change, the sonographer has to make that change. And that’s different than most machines.* Those are the two major considerations, but they are certainly workable and we’ve taught all our sonographers about them.... (Emphasis added.)

In every case where inappropriate Nyquist limits were used, they could have easily been adjusted to over 50 cm/sec -- the least acceptable Nyquist limits identified in the *ASE Standards*.

Moreover, the Court finds that Dr. Mancina’s assertion that he regularly uses Nyquist limits in the 40 cm/sec range not to be credible. As noted, Dr. Mancina supervised the performance of approximately 20,000 echocardiograms in connection with phen-fen litigation across the United States. In guidance

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A. My answer is I can make a clinical decision at low 40s as well as at 50s or 60s that’s accurate.

memoranda written in 2002 and 2003 and given to the sonographers working with him, Dr. Mancina directed these individuals to:

***Never*** test with a color scale [Nyquist limit] of less than 51 [cm/sec] (preferably test in the range of 60's).

\* \* \* \*

***Do not ever*** use a color scale [Nyquist limit] of less than 51. Show the jet primarily in live motion and replay in live motion, rather than clips stored of the jet. (Emphasis added.)

The Nyquist settings articulated by Dr. Mancina are in accordance with the *ASE Standards* and the Weyman Text. This plainly indicates what Dr. Mancina's clinical practice was in 2002 and 2003. His present testimonial claims in light of these memoranda plainly are entitled to little or no weight.

Plaintiffs' broader attacks on standard setting for parameters such as Nyquist limits fair no better. Miele challenged the mathematical underpinnings for the claim that low Nyquist limits can significantly affect the apparent area of a regurgitant jet. In his view, while the mathematics plainly support the claim that as a Nyquist limit falls the regurgitant jet area enlarges at an increasing rate, the formula is useless in real world situations.<sup>5</sup> Miele believes that there are simply too many variables in the real world -- *in vivo* -- to accept that these mathematical truths are applicable.

The Court rejects Miele's claims that Nyquist limits are nothing but a function of clinical judgment. Instead, it accepts Dr. Thomas' testimony that low Nyquist limits have a significant distorting effect on regurgitant jet area measurements. Dr. Thomas acknowledges that "chamber constraint, coflow, orifice irregularity, unsteady flow and spatial, temporal, and velocity resolution issues in the ... [echocardiographic machine]" may also influence regurgitant jet size. Nevertheless, he was steadfast that as Nyquist limits decrease, jet area size increases at an increasing rate.

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<sup>5</sup> Miele himself accepted the theoretical physics that a decreasing Nyquist limit caused the regurgitant jet area to increase at an increasing rate.

JUDGE WALSH: Does a decreasing Nyquist, all things equal, cause the regurgitant jet area to enlarge at an increasing rate:

THE WITNESS: Yes, it does. In fact, that's one of the first points I made this morning, that I agree with that premise.

Dr. Thomas put it this way:

As I derived in my 1991 *Circulation* manuscript, for an unconstrained axisymmetric jet, jet area should rise as the inverse square of the low-velocity cut-off (generally a percentage of the Nyquist limit, whether this is based on discretization criteria or wall-filter criteria, since both are tied to the Nyquist limit in practical terms). This would produce a strongly curvilinear increase in jet area with falling Nyquist. It should be emphasized that the vast majority of jets under consideration in the Fen Phen litigation are indeed unconstrained, or “barely” constrained, in that they do not come anywhere near filling the receiving chamber, be it the left atrium for mitral regurgitation or the left ventricle for aortic regurgitation. Therefore, we anticipate the inverse of the first power of the low-velocity cut-off, this would still present a curvilinear increase in jet area with falling Nyquist velocity, as the second derivative of  $1/x$  is  $2/x^3$ , which remains strongly curved upwards (positive curvature) as it approaches 0 velocity. (*A perhaps simpler way of seeing this is to note that if jet area is proportional to  $1/\text{Nyquist velocity}$ , then going from 60->50 cm/sec leads to a 20% increase in jet area, while going from 50->40 cm/sec leads to a 25% increase in an already enlarged jet area, thereby confirming that it grows faster and faster as Nyquist falls.*) As to the issue of whether the increase in jet area when lowering Nyquist ever flattens out, this is only a possibility with much larger jets that are coming close to filling the receiving chamber. Clearly, a jet can grow no larger than the chamber into which it is flowing, no matter how low the Nyquist velocity. So for very severe regurgitation, we would indeed expect that jet area would rise with lowering the Nyquist limit, but would eventually flatten out and ultimately level out at the full size of the left atrium or left ventricle. (Emphasis added.)

Dr. Thomas’ observations, which are supported by science and the scientific community, make it abundantly clear that Nyquist limits in the 40 cm/sec to 49

cm/sec range significantly distort and enlarge regurgitant jet areas and should not be accepted by the Court. To quote Dr. Mancina in this regard, a sonographer should “[n]ever test with a color scale [Nyquist limit] of less than 51 [cm/sec] (preferably test in the range of 60’s).”

The Court finds that in many instances the techniques used in acquiring the echocardiographic images fell so far below appropriate practice as to make the data reported and conclusions made by plaintiffs’ experts virtually worthless in either diagnosis or treatment. With respect to the forty-seven (47) plaintiffs included in this Letter Opinion, the experts appointed by the Court concluded that with respect to fifty-one percent (51%) of them, the echocardiograms were so technically inadequate that reasonable medical conclusions could not be drawn from them.

Plaintiffs were aware that the qualifying echocardiograms in issue would be used to support the opt-outs sought. Dr. Mancina’s memoranda were also instructive on this point in which he told the sonographers working with him:

I know that you are all aware we are in the last month of the [phen-fen] ... project and we are doing some primary testing as well as some re-testing. In every case I’d like you to be aware that *the final tests are the only opportunity clients will have to make it into the matrix....* (Emphasis added.)

As will be seen, however, in the forty-seven (47) cases reviewed here, many of the submitted echocardiograms were of such poor quality or were interpreted in a manner so plainly at odds with good medical practice that they cannot, as a matter of law, support those plaintiffs’ claims to qualify as FDA Positive. Overall, the experts appointed by the Court opined in seventy-two percent (72%) of the cases that the FDA Positive mitral or aortic regurgitation determinations made by Dr. Mancina were not medically reasonable.

The findings with respect to the forty-seven (47) plaintiffs follow in the next section of this Letter Opinion. Where credibility determinations in these individual cases are made, they are reflected in the findings reported below.

### III

#### A. MONYA A. ADAMSON

Adamson relies on an April 14, 2000 echocardiogram performed by Dr. Charles F. Dahl. Dr. Dahl found that Adamson had mild aortic regurgitation (“MAR”). No quantitative information about the regurgitation was provided nor was it clear from the report that CAS criteria were used.

The April 14, 2000 echocardiogram was reviewed by three (3) experts: Dr. Wangenheim, Dr. Saric and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate.

Drs. Saric and Mancina concluded that Adamson has MAR. Dr. Saric measured a JH of .25 cm and an LVOT of 1.95 in the PLAX view, yielding a JH/LVOT of 13%. Dr. Mancina failed to measure in the PLAX view, claiming that it was not diagnostic. Instead, he measured in the apical 3 chamber view and found a JH/LVOT ratio of 23%.

Dr. Wangenheim disagreed. He found that the JH/LVOT “is clearly less than 10% and not FDA positive.” Dr. Wangenheim conceded that there was some aortic regurgitation, but did not believe that it reached the 10% figure and that the jet observed was not holodiastolic.

The Court finds that the PLAX view is available and that Dr. Mancina improperly measured the apical 3 chamber view. Nevertheless, the Court finds that Wyeth failed to establish that no reasonable medical opinion that Adamson was FDA positive could be based on this echocardiogram. Dr. Saric measured the jet in the PLAX view and concluded that Adamson had MAR. The Court reviewed the media and believes that continuous wave (“CW”) Doppler demonstrates a high velocity jet through at least half of the diastolic cycle. A review of the evidence demonstrates that it would be medically reasonable to conclude that Adamson has MAR.

#### B. KIMBERLY M. ALTHAUSEN

Althausen relies on a September 15, 2002 echocardiogram report of Dr. Richard P. Brown. Dr. Brown found Althausen had MAR using CAS criteria -- JH/LVOT = 22%. No specific measurements of JH or LVOT were given. Dr. Brown found that “[t]he technical quality of this examination is good.”

The September 15, 2002 echocardiogram was reviewed by three (3) experts: Dr. Wangenheim, Dr. Saric and Dr. Mancina. Dr. Saric found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Drs. Wangenheim and Mancina believed that the quality of the echocardiogram was sufficient for review, though Dr. Mancina conceded that this was a “suboptimal study.”

Dr. Wangenheim reported that there was no indication of a holodiastolic jet. He noted that:

Viewing multiple cardiac loops, no consistent holodiastolic jet or aortic insufficiency is visualized in the PLAX view. I also reviewed the only freeze-frame supplied on the study. The severity of aortic insufficiency cannot be determined from this single freeze frame. However, several cardiac cycles that follow are not holodiastolic, are clearly less than ten percent of the left ventricular outflow tract and are not consistent with FDA Positive aortic insufficiency. Additionally, a Doppler examination of the descending aorta at frame 11:56:34 confirms the absence of true aortic regurgitation, revealing minimal flow reversal that occupies only the first third of diastole. Finally, at frame 11:57:30, even though the color Doppler examination was conducted with a low Nyquist limit of 51, no signal of aortic insufficiency is visualized.

Dr. Mancina disagreed, finding that the aortic regurgitation, when measured by JH/LVOT, was 19.7%. However, he conceded on cross-examination that the jet was not holodiastolic and, at best, occurred in two (2) frames.<sup>6</sup>

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<sup>6</sup> Dr. Mancina testified as follows:

BY MR. WHEELER:

Q. Dr. Mancina, wouldn't you agree that we've been through enough cycles to cover two, perhaps three diastolic cycles of the heart?

A. Well, there are two spots that I see that have a fragment of the jet and as you know, the heart translates through the chest and it changes its relationship to the transducer, and what you're seeing here is a region where it's more difficult to see the jet but the jet is seen.

Q. In two frames?

A. In two frames.

The Court finds that Wyeth has established that the gain plainly was set too high on this echocardiogram. Thus, the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. It also finds that Wyeth prevails on the substance of the echocardiogram. Here, it is evident that no reasonable medical opinion that Althausen has MAR could be based on this echocardiogram. The Court finds that a jet observed is not holodiastolic. As Dr. Saric noted:

JUDGE WALSH: And did you proceed to examine it to determine whether there was FDA-positive aortic regurgitation by color flow?

THE WITNESS: Yes, I did try to isolate the AI jet; however, JH cannot be measured accurately when color gains are too high and I just don't want to condone a bad practice, but I also concluded that the AI or aortic regurgitation appears trace even with the high color gain settings.

JUDGE WALSH: So, in essence, you were saying you couldn't quantify comfortably any AI jet because of the high color gain, but because you could observe the jet even in its enhanced place, you were satisfied that at most it was trace?

THE WITNESS: Yes, your Honor.

### **C. JUDY ALVEY**

Alvey relies on a June 28, 2002 echocardiogram and a report by Dr. Robert M. Applebaum. Dr. Applebaum found that Alvey had MAR using CAS criteria -- JH/LVOT = 15%. The quality of the echocardiogram was listed as "fair."

The June 28, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Both Drs. Saric and Chen determined that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular disease could be drawn from it. Dr. Saric found that the "[c]olor gain settings are very high which increases apparent size of any jet." Dr. Chen concurred and noted: "This study has extremely high color Doppler gain settings, as evidenced by excessive color speckles and artifacts with a firework appearance, in the PLAX view, which renders assessment of the degree of aortic regurgitation unreliable."

Dr. Mancina disagreed that the study was technically inadequate but did agree that the gain setting exceeded the acceptable range set out in the instructions given to his sonographers:

BY MR. WHEELER:

Q. Dr. Mancina, before we leave this Apical 5 view, you would have to agree, would you not, sir, that the gain in this view is excessive involving color speckling into the tissue which would be violative to your instruction to sonographers in these cases, correct?

A. That's correct.

The gain setting was 20, well above the maximum gain he approved for use by Dr. Mancina's sonographers.

Dr. Saric could not unequivocally identify an aortic regurgitant jet in the PLAX view though he believed that some regurgitation was present from examination of the echocardiogram. Dr. Chen, too, acknowledged that there was a small amount of aortic regurgitation. Neither believed it approached MAR. As Dr. Chen observed:

As noted above ..., this study is technically deficient, due to extremely high color Doppler gain settings, particularly in the PLAX view. In real-time images, on pages #3/65 during the loop of 10:18:42-43, there appears to be a tiny AR jet intermingled with excessive color artifacts due to extremely high color Doppler gain, which makes assessment of AR unreliable. "AR" jets measured on still frames (page 4/65, page 5/65, page 5/65) by the technician did not have corresponding real-time images and cannot be evaluated in the context of extremely high color Doppler gain settings which significantly exaggerate JH or jet size.

Dr. Mancina claimed that MAR was present but inexplicably failed to measure any regurgitant jet in the PLAX view.

BY MR. WHEELER:

Q. And you would agree, would you not, that the PLAX view is available on this study, yet you chose to make measurements in an apical view, correct?

A. That's correct.

Dr. Mancina found a JH/LVOT of 14% but made his measurements in the apical 5 chamber view. This is not a permitted view. Thus, there is no evidence that Alvey has MAR using CAS criteria.

The Court finds that Wyeth has satisfied its burden and has shown that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. In any case, the evidence shows that no permissible measurement of MAR was made by any witness since Dr. Mancina measured Alvey's alleged aortic jet in the wrong view. Finally, the evidence makes it clear that no reasonable physician could come to the conclusion that Alvey has MAR based on examination of the PLAX views in this echocardiogram.

#### **D. GWENDOLYN ANDERSON**

G. Anderson relies on an October 16, 2002 echocardiogram and a November 24, 2002 report by Dr. Marcus Brann. Dr. Brann found that G. Anderson had moderate aortic regurgitation ("MMAR") using CAS criteria -- JH/LVOT - 32%. Dr. Brann reported that "[t]his is a technical[ly] adequate quality of study."

The October 16, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Both Drs. Saric and Chen found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Saric noted:

Nyquist limit was set to 46 cm/sec throughout the study. This setting exaggerates the amount of color on the screen thus making any regurgitant jet larger than it truly is. Therefore, the study methodology does not conform to the recommendation of the American Society of Echocardiography regarding both the Nyquist limit & color gain settings ("Stadand (sic) [Standard] technique is to use a Nyquist limit of 50-60 cm/sec, and color gain

that just eliminates random color speckle from non-moving regions.” p. 778, J Am Soc Echocardiog 2003: 16:777-802).

Dr. Chen concurred.

Dr. Mancina disagreed that the technical quality precluded a meaningful diagnosis. He conceded that the Nyquist limit was below 50 cm/sec but argued that this setting would not hamper a diagnosis of MAR.<sup>7</sup> Dr. Mancina saw MAR here and measured it at 15.6% -- less than half the percentage claimed by Dr. Brann.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. For the reasons already discussed in this Letter Opinion, a Nyquist limit of 46 cm/sec has a significant distorting effect on jet size. In addition, the echocardiogram clearly is overgained. The combination of these two (2) factors makes the echocardiogram technically unreliable. It is also worth noting that this inappropriate Nyquist setting was unnecessary because the probe depth was only 16.2 centimeters and, therefore, the Nyquist limit could have been set at 61 cm/sec.

## **E. MARIANNE ANDERSON**

M. Anderson relies on a November 21, 2002 echocardiogram and report of Dr. Raymonda Rastegar. Dr. Rastegar found that M. Anderson had MAR using CAS criteria -- JH/LVOT = 20%. The quality of the echocardiogram was listed as “fair.”

The November 21, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Saric and Dr. Mancina. Both Drs. Saric and Goldman found that

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<sup>7</sup> Dr. Thomas observed that in G. Anderson’s

parasternal long axis images, the Nyquist limit was set at 46 cm/sec despite an imaging depth of 16.2 cm, which should have allowed a theoretically maximal Nyquist limit of 61.8 cm/sec (maximum on the Cypress machine of 61 cm/sec). Furthermore, the left ventricular outflow tract (LVOT) could have been fully interrogated at a depth of 10.8 cm, which would have allowed a theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec. For imaging in the apical 4-chamber view, the Nyquist limit was similarly set at 46 cm/sec despite depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec).

the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Goldman best summarized their conclusion: “The echocardiogram had an excessive color Doppler gain setting and a borderline Nyquist setting of 51 cm/sec at a 10.8 cm depth. Despite being acquired with poor technique, no sustained holodiastolic turbulent jet of aortic insufficiency is present.”

Dr. Mancina disagreed. According to him, M. Anderson has MAR with a JH equal to .23 centimeters and an LVOT equal to 1.737 centimeters or 13.2%. Dr. Mancina conceded that the gain was high and the Nyquist was inexplicably low. He agreed the Nyquist could have been raised at least to the 70 centimeter range given the probe depth of only 10.8 centimeters.

The Court finds that Wyeth easily satisfied its burden to demonstrate that the echocardiogram was not conducted in a technically adequate manner. The Court finds that no reliable medical conclusions regarding valvular regurgitation could be drawn from review of this echocardiogram.

## **F. SHERYL A. ANDERSON**

S. Anderson relies on a June 21, 2002 echocardiogram and a report of Dr. Scott L. Roth. Dr. Roth found S. Anderson had MAR using CAS criteria --  $JH/LVOT = 20\%$ . The sonographer reported severe aortic regurgitation (“SAR”) of 56%.

The June 21, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Both Drs. Saric and Chen found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular disease could be drawn from it. Dr. Saric reported that the “[c]olor gain settings were too high” exaggerating the apparent size of any observed jet. Dr. Chen concurred with Dr. Saric with respect to the gain setting and added the following with respect to S. Anderson’s claimed pathology.

As noted above, there is a technical deficiency of significantly high color Doppler gain settings which results in excessive color speckles and artifacts with color overlaying static tissues, and thereby exaggerates the jet size or jet height and makes assessment of the

degree of aortic regurgitation unreliable. In addition, the “AR jets” selected and measured by the technician are improper. The JH was not measured just below the aortic valve or at the narrowest point and the LVOT was not measured on the frame with a maximal LVOT.

Moreover, Dr. Chen noted the regurgitant jet seen in this echocardiogram was not holodiastolic.

Dr. Mancina disagreed that the gain distorted the jets he observed and claimed to measure a JH of .30 centimeters and an LVOT of 2.2 centimeters leading to a JH/LVOT = 13.6%. But the echocardiogram makes it clear that the gain setting violated his own directive that it “always be in the range of 6-11.” Moreover, he conceded that the jet he measured was distal from the aortic valve annulus.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner because of the overgaining. Thus, no reliable medical conclusions respecting the presence and severity of valvular disease could be drawn from its review. Moreover, no reasonable medical conclusion that S. Anderson has MAR can be gleaned from it. To the extent it can be read, it appears to show a non-holodiastolic jet which disappears shortly into diastole.

## **G. TERILYN ANDERSON**

T. Anderson relies on a June 19, 2002 echocardiogram and a report by Dr. Scott L. Roth. Dr. Roth found T. Anderson had MAR using CAS criteria -- JH/LVOT = 22%. The sonographer initially found JHs of .64, .50 and .68 and an LVOT of 1.4 cm -- computing to a JH/LVOT of almost 50%.

The June 19, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Drs. Saric and Chen agreed that the gain settings were too high. Dr. Chen believed that the high gain setting required a judgment that the echocardiogram was not conducted in a technically adequate manner. Dr. Saric concurred that the gain setting was too high but believed “a valid medical conclusion in this particular patient” could be drawn from it. In Dr. Saric’s view, “[e]ven allowing for high color gain settings which exaggerate any jet, I think that in this particular patient the AI jet is substantial enough to be graded as being more than trace. Persistent AI jet is seen on color Doppler in

PLAX, A5C and A4C views as well as on spectral Doppler on page 31.” Dr. Saric measured a JH and LVOT and concluded T. Anderson has MAR with a JH/LVOT of 12%.

Dr. Mancina agreed with Dr. Saric that T. Anderson has MAR but disagreed that the gain setting was too high. Dr. Mancina measured a JH of .38 centimeters and an LVOT of 1.84 centimeters which computes to 20.6%. His denial that the echocardiogram is overgained is belied by the instruction given to his sonographers. Here, the gain setting was 14, well above the 6 to 11 range which he required of his own employees.

The Court finds that Wyeth has not established that this echocardiogram was so flawed that no reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. While the Court finds that this echocardiogram is marginal at best, it is not prepared to find, in the face of Dr. Saric’s testimony, that no reliable medical conclusions about the presence and severity of valvular disease could be drawn from it.

## **H. LaNECE ANDREASON**

Andreason relies on a June 20, 2002 echocardiogram and report of Dr. Scott L. Roth. Dr. Roth found that Andreason had MAR using CAS criteria -- JH/LVOT = 14%.

The June 20, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Both Drs. Saric and Chen determined that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Saric observed that the

Nyquist limit was set to 46 cm/sec in FDA relevant views. This setting exaggerates the amount of color on the screen thus making any regurgitant jet larger than it truly is. Therefore, the study methodology does not conform to the recommendation of the American Society of Echocardiography regarding both the Nyquist limit & color gain settings (“Stadand (sic) [Standard] technique is to use a Nyquist limit of 50-60 cm/sec, and color gain that just eliminates random color speckle from non-

moving regions. p. 778, J Am Soc Echocardiog 2003: 16:777-802).

Dr. Chen concurred.

Dr. Mancina disagreed. In his view, the Nyquist limits and gain settings were appropriate in this clinical setting. Dr. Mancina measured a JH of .3 centimeters and an LVOT of 1.95 centimeters which computes to 15.3%.<sup>8</sup>

The Court finds that Wyeth has easily satisfied its burden to show this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The Court has already discussed the significant distortion to jet size caused by low Nyquist limits and high gain settings and need not repeat these observations here.<sup>9</sup>

## **I. LAURA AYEN**

Ayen relies on a December 6, 2002 echocardiogram and a report by Dr. Arthur Schwartzbard. Dr. Schwartzbard found Ayen had MAR using CAS criteria -- JH/LVOT = 14.3%. The sonographer noted a JH/LVOT of more than double this. The quality of the echocardiogram was listed as “fair.”

The December 6, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Dr. Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions concerning the presence and severity of valvular regurgitation could be drawn from it. He noted that this was a

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<sup>8</sup> Dr. Thomas noted that

[f]or LaNece Andreason, in whom mild aortic regurgitation is claimed (14%), the Nyquist limit was set at 46 cm/sec despite a depth of 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec), and aortic regurgitation could have been imaged at 10.8 cm (theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit similarly was set at 46 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec); the depth actually could have been 13.5 (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec).

<sup>9</sup> It is noteworthy that these low Nyquist settings were set at 46 cm/sec when the probe depth was only 13.5 cm. At that depth, the Nyquist could have been set over 70 cm/sec. In the Court's view, only carelessness or intentional conduct can explain this low Nyquist setting.

[p]oor study quality in the PLAX view. [There is an] [e]xcessively high color Doppler gain setting in two of three PLAX views, precluding reliable assessment of aortic regurgitation. In the remaining PLAX view, the LVOT and aortic valve imaging quality is so poor and the view is so oblique that reliable assessment of the degree of aortic regurgitation is not possible. In the apical views, Nyquist velocity was set too low (46 cm/s[ec]) and color Doppler gain was set too high, precluding reliable evaluation of degree of aortic regurgitation in that view as well.

Dr. Saric concurred as to the quality of the study, but believed that “a valid conclusion that AI (aortic regurgitation) is no more than trace can still be made.”

Dr. Mancina disagreed, claiming that the gain settings were appropriate in this clinical context. A review of the echocardiogram, however, discloses that the gain was set at 14, well above the 6-11 range which Dr. Mancina counseled should “always” be used. Dr. Mancina noted a JH of .32 centimeters and an LVOT of 2.25 centimeters which computes to 14.2%.

The Court finds that Wyeth has satisfied its burden on two (2) scores. First, the Court is satisfied that the echocardiogram was not conducted in a technically adequate manner. There simply was too much gain. The Court also believes that no reasonable physician could conclude on the basis of this echocardiogram that Ayen has MAR. The measurements made by Dr. Mancina were done on a non-aliased phenomenon appearing at a marginal Nyquist limit of 51 cm/sec. The measurement performed by Dr. Saric showing a JH/LVOT of 7% is a more representative measurement of Ayen’s trace regurgitation, if it can be reliably measured at all.

## **J. PAMELA BEDDOES**

Beddoes relies on a June 19, 2002 echocardiogram and a report by Dr. Robin S. Freedberg. Dr. Freedberg found Beddoes had MAR using CAS criteria -- JH/LVOT = 22%. The quality of the echocardiogram was listed as “good.”

The June 19, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Both Drs. Saric and Chen concluded that this echocardiogram was not conducted in a technically adequate manner such that

reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Saric noted that the

Nyquist limit was set too low to 46 cm/sec and color gains were too high in all FDA relevant views. These settings exaggerate the amount of color on the screen thus making any regurgitant jet larger than it truly is. Therefore, the study methodology does not conform to the recommendation of the American Society of Echocardiography regarding both the Nyquist limit & color gain settings (“Stadand (sic) [Standard] technique is to use a Nyquist limit of 50-60 cm/sec, and color gain that just eliminates random color speckle from non-moving regions. p. 778, J Am Soc Echocardiog 2003: 16:777-802).

Dr. Chen concurred.

Dr. Mancina disagreed and claimed that the high gain setting, in this case 21, and low Nyquist did not affect the ability to diagnose aortic regurgitation.<sup>10</sup> However, on cross-examination, he conceded that the gain here was very high and the low Nyquist could have easily been adjusted to .70 cm/sec.

BY MR. WHEELER:

Dr. Mancina, I think everyone present in the courtroom would agree that there is significant speckling of color into the tissue on this study?

A. Yes.

Q. You would agree that the gain is excessive?

A. Gain is high here.

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<sup>10</sup> Dr. Thomas noted that for Beddoes,

for whom mild aortic regurgitation is claimed (22%), the Nyquist limit was set at 46 cm/sec despite a depth of 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec), and aortic regurgitation could have been imaged at 10.8 cm (theoretical/Cypress maximal Nyquist limit of 92.6/85 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit similarly was set at 46 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec). I also note that the purported mitral regurgitation is measured in diastole (pages 24-26).

Q. And the Nyquist limit is 46 at a depth, maximum depth at 13.5 sonometers?

A. That's correct.

Q. So the record will be clear and I think it is from previous studies, you would agree that if the technician had chosen to do so and perhaps should have chosen to do so that the Nyquist on this particular image could have been in excess of 60?

A. That's correct.

The Court finds that Wyeth has easily satisfied its burden of showing that this echocardiogram was not conducted in a technically adequate manner such that reliable medical opinions regarding the presence and severity of valvular regurgitation could be drawn from it. The gain settings and Nyquist limit doom this echocardiogram from the outset.

#### **K. LAURIE BENSON**

Benson relies on a November 25, 2002 echocardiogram and report by Dr. Stanley S. Schrem. Dr. Schrem found Benson had MAR using CAS criteria -- JH/LVOT = 19%. The quality of the echocardiogram was listed as "fair."

The November 25, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Saric and Dr. Mancina. Dr. Stern found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Stern noted that:

The color gain is set too high, causing extreme "speckling" throughout the images. In addition, the Nyquist setting of 51 cm/sec is borderline and really should be set higher, especially in the parasternal long axis view. These improper settings make it medically unreasonable to rely on this echocardiogram or to make any measurement or diagnosis from it.

Dr. Saric found the study to be technically adequate, but found no evidence of aortic regurgitation in the PLAX view. But he did find evidence of MAR in the apical long axis view. His testimony on these scores is instructive.

JUDGE WALSH: Did you look at Ms. Benson's echocardiogram to determine whether it was conducted in a technically adequate manner that reliable medial conclusions regarding valvular regurgitation could be drawn from it?

THE WITNESS: Yes, I did examine it and I found that the study is acceptable.

JUDGE WALSH: No mitral regurgitation claim was made but an aortic regurgitation claim was made.

Did you examine the parasternal long axis view to determine whether it was available on the echocardiogram?

THE WITNESS: Yes, your Honor. I found that the parasternal long axis was available but then I also noted there was no persistent jet of atrial regurgitation in any of the three Color Doppler claims in the parasternal long axis view so technically the diagnosis of FDA-positive atrial regurgitation cannot be established.

JUDGE WALSH: And actually what you wrote is there is on, so for the sake of good order, can we change that? There is no consistent jet of AR in any three Color Doppler clips in the PLAX view.

THE WITNESS: I apologize for the typo.

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JUDGE WALSH: .... Any other comments you want to make with respect -- I think you answered eight and you took a measurement as well. I'm sorry you answered Question 8, 9 and took a measurement which are reflected in 10. So why don't you tell us in narrative fashion what the significance is there?

THE WITNESS: So let's say that -- okay. I'll say this is no parasternal long axis view. But maybe I can use apical three chamber view which is the second best option and I use the electronic calipers within Access Point 2000 software for JH I used apical three chamber view on Page 47, Frame 29 for LVOT I accepted the sonographer's measurements.

So I found that JH and LVOT ratio was 12 percent. So there appears to be mild atrial regurgitation apical

three chamber view, but this was not the parasternal long axis view so --

JUDGE WALSH: It's well-known, I take it, Doctor, that the apical three chamber view tends to exaggerate the regurgitant jet by -- because of the positioning of the transducer relative to the blood flow.

THE WITNESS: I would say that the parasternal long axis view is the preferable view, and the preferable view to do the JH over LVOT measurements.

JUDGE WALSH: All right. Could a physician acting reasonably with your skill sets conclude that Ms. Benson had FDA-positive aortic regurgitation using the PLAX views?

THE WITNESS: Using the PLAX views, I really have to say that technically you cannot establish the atrial regurgitation. The diagnosis of FDA-positive atrial regurgitation, but I'm also a clinician and I look at the apical three chamber view but technically on the parasternal long axis view, no.

JUDGE WALSH: Well, all right, let's make a record then so that whatever is decided, we have your complete opinion. Looking at the apical long axis view, would it be medically reasonable to diagnose this patient with FDA-positive aortic regurgitation.

THE WITNESS: If I confine myself to the apical three chamber view, I would say yes.

JUDGE WALSH: What about overall taking the echocardiogram in its entirety?

THE WITNESS: I would say probably yes.

Dr. Mancina agreed with Dr. Saric that the echocardiogram was technically adequate and claimed to measure a JH of .34 centimeters and an LVOT of 2.1 centimeters which computes to 14.7%. However, on cross-examination, Dr. Mancina was unable to identify the frame he measured.

The Court finds that Wyeth has established that there is no evidence of aortic regurgitation in the PLAX view. The PLAX view is the preferred view and must be used if it is available. Feigenbaum 6<sup>th</sup> Edition Text makes it clear that the apical long axis view tends to exaggerate the jet width.

The width of an aortic regurgitant jet is often greater from an apical view compared with a parasternal view. This is because the jet's width recorded from a parasternal projection depends on axial resolution, whereas the same dimension recorded apically will rely more on lateral resolution, resulting in the appearance of a wider jet.

Feigenbaum 6<sup>th</sup> Edition Text at 296-298. Dr. Saric testified that as a clinician and looking at all views, Benson “probably” has MAR. But he was equally clear that “[u]sing the PLAX view, I really have to say that technically you cannot ... [diagnose MAR].”

## **L. LYNETTE BINGHAM**

Bingham relies on a July 18, 2002 echocardiogram and report of Dr. Robin S. Freedberg. Dr. Freedberg found Bingham had MAR using CAS criteria -- JH/LVOT = 17%. The quality of the echocardiogram was listed as “fair.”

The July 18, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Saric and Dr. Mancina. Dr. Chen determined that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. He based his conclusion on the “[e]xtremely high color Doppler gain settings combined with relatively low Nyquist velocity (51 cm/s[ec]) [which] produced excessive color artifacts and speckles in this study and also exaggerated regurgitant jet size. Thus, the degree of valvular regurgitation cannot be reliably measured.”

Dr. Saric concurred that the color gains were excessive but believed that the echocardiogram could be used to exclude a diagnosis of MAR. He noted that “[o]f the 3 color Doppler clips in the PLAX views (pages 3, 4 & 27), the AR jet is unequivocally identifiable only on page 27. Despite high color gains, JH/LVOT is still <10%.”

Dr. Mancina acknowledged that the gain was set at 12 which was above the limits placed on his sonographers. Nevertheless, he did not believe the echocardiogram was overgained. He measured a JH of .26 centimeters and an LVOT of 1.94 centimeters which computes to 13.4%. He conceded that the

marginal Nyquist of 51 cm/sec could have been raised to 71 cm/sec without altering the probe depth of 13.5 centimeters.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical opinions regarding the presence and severity of valvular regurgitation could be drawn from it. Moreover, Dr. Saric's measurement of JH/LVOT = 8% was the maximum possible measurement given the echocardiogram's infirmities. The Court is satisfied that Wyeth has established that no reasonable physician would conclude that Bingham has MAR using CAS criteria.

#### **M. DEBORAH BOOTS**

Boots relies on a November 15, 2002 echocardiogram and report by Dr. Gregory T. Anthony. Dr. Anthony found Boots had MAR but it is unclear whether CAS criteria were used. Virtually no measurements were provided.

The November 15, 2002 echocardiogram was reviewed by three (3) experts: Dr. Schwartz, Dr. Gopal and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate.

Both Drs. Gopal and Schwartz found no aortic regurgitation in the PLAX views. Dr. Gopal noted some aortic regurgitation in the apical long axis views. She observed:

Parasternal views did not reveal any aortic regurgitation. Only the apical views revealed trivial aortic regurgitation that did not meet FDA positive criteria. Aortic regurgitation jet was thin and fleeting lasting for no more than 1 or 2 videoframes in diastole. Therefore, FDA positive criteria are not met. The initial qualifying echocardiogram did not specify any jet height/LVOT height ratios to justify the claim of FDA positivity. Even though the frames that purported to show a jet height ratio of 17% were mentioned in Dr. Mancina's report, they were only apical frames and therefore do not fall strictly into the criteria set forth by the court with regard to the parasternal long axis view.

Even in the apical long axis, Dr. Gopal measured a JH/LVOT of between 6.8% and 9.1%.

Dr. Mancina disagreed. In the PLAX view, Dr. Mancina claimed a JH of .31 centimeters and an LVOT of 1.95 centimeters computing to 15.9%. Dr. Mancina originally claimed a JH/LVOT of 17% measured in the apical long axis views, implying that the PLAX view was unavailable.

The Court has examined the echocardiogram and considered the testimony of these experts. It is satisfied that Wyeth has established there is no aortic regurgitation seen in the PLAX view. Since the PLAX view was available, it is the only approved view.

## **N. KIM W. BOWLDEN**

Bowlden relies on a June 20, 2002 echocardiogram and report by Dr. Scott L. Roth. Dr. Roth found that Bowlden had MAR using CAS criteria -- JH/LVOT = 19%.

The June 20, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Gopal and Dr. Mancina. Dr. Chen found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Chen observed that “[h]igh color Doppler gain settings with excessive color artifacts and color speckles exaggerate regurgitant jet size and render assessment of the degree of aortic regurgitation unreliable.”

Dr. Chen made other substantial criticisms.

As noted ..., this study is technically deficient, due to excessively high color Doppler gain settings which exaggerate jet size and make assessment of regurgitation using JH/LVOT criteria unreliable. In addition, JH was measured improperly by the technician. JH was not measured just below the aortic valve and was measured beyond the jet’s anterior and posterior edges. No reasonable medical judgment can be made about whether there is FDA positive aortic regurgitation in this case because of the technical deficiency.

Dr. Gopal agreed with Dr. Chen that the echocardiogram was overgained. Still, she believed MAR could be seen and measured. She stated:

Though the overall color gain is somewhat higher than desirable in the parasternal long-axis view, nevertheless, a clear aortic regurgitant diastolic jet is noted in image 4 that meets FDA positive criteria. The aortic regurgitation jet is confirmed on parasternal short axis and apical views as well.

Dr. Gopal measured a JH of 3 millimeters and an LVOT of 21 millimeters, yielding a JH/LVOT = 14.3%.

Dr. Mancina found this study to be technically adequate though the gain of 13 exceeded his directions to his technicians about gain settings. He also found MAR with a JH of .36 centimeters and an LVOT of 2.24 centimeters. This implies a JH/LVOT of 16.1%. As noted in the transcript, the Court has serious problems with Dr. Mancina's measurements of this aortic jet. In the Court's view, it should have been measured closer to the jet's origin.

Nevertheless, the Court believes that Wyeth has not established that the technique here was so far outside appropriate norms that it cannot support the opt-out here. While it is a close question whether MAR is present here, the Court finds that a reasonable physician could find that Bowlden has MAR.

## **O. KAYELA J. BRADFORD**

Bradford relies on a July 12, 2002 echocardiogram and report of Dr. John E. Lassetter. Dr. Lassetter found that Bradford had MAR using CAS criteria -- JH/LVOT = 17%. The echocardiographer initially found SAR with JH/LVOT = 49%.

The July 12, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Gopal and Dr. Mancina. Both Drs. Gopal and Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Chen observed that "[t]his study has excessively high color Doppler gain settings, particularly in the parasternal long axis view, making assessment of valvular regurgitation unreliable." Dr. Gopal concurred.

Dr. Mancina disagreed that the study was of poor technical quality though review of the study shows the color gain was excessive. The gain, which was set at 15, is well above that which Dr. Mancina condoned in his memoranda.

Both Drs. Gopal and Chen reviewed the flawed echocardiogram on its merits. Both concluded that evidence of MAR was not present. Dr. Chen noted:

[T]his study is technically inadequate for accurate assessment of aortic regurgitation. In addition, there is no definite aortic regurgitant jet which lasts even the majority of the period of diastole. Furthermore, although the PLAX view was available, the “JH,” which was measured by the technician in the apical 3-chamber view on still frames (14:10:10 and 14:10:49), is not measured on an aortic regurgitant jet. On the frame of 14:10:10, the time bar on the EKG tracing was before the T-wave (*i.e.*, in systole). On the frame of 14:10:49, the “AR” jet measured does not have a developed AR jet appearance (*i.e.*, that of a jet stemming from aortic valve with a narrowest portion just below or at the aortic valve).

Dr. Mancina claimed to have measured a JH/LVOT ratio of 16.5%. However, during cross-examination, he conceded that it was not clear whether the frame was in systole or diastole. In any case, Dr. Mancina admitted that the loop he studied showed that the so-called jet was present in only one (1), or at most two (2), frames.

The Court finds that Wyeth has satisfied its burden to demonstrate that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Moreover, Wyeth has established that review of the echocardiogram produces no reliable medical evidence that Bradford has MAR nor could a reasonable physician so conclude.

## **P. KAREN I. BRAILSFORD**

Brailsford relies on an August 20, 2002 echocardiogram and report of Dr. Robin S. Freedberg. Dr. Freedberg found that Brailsford had MAR using CAS criteria --  $JH/LVOT = 18\%$ . The quality of the echocardiogram was listed as “good.”

The August 20, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Gopal and Dr. Mancina. Both Drs. Gopal and Chen found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Gopal reported that “[c]olor gain was excessive in the parasternal long axis view as evidenced by speckling and may have erroneously increased the apparent severity of aortic regurgitation.”<sup>11</sup> As a

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<sup>11</sup> The Court is aware that Dr. Gopal evaluated the echocardiogram despite her conclusion that the echocardiogram was not technically adequate. Ultimately, she found only trace aortic regurgitation. However, she noted that a physician acting reasonably might conclude otherwise. Dr. Gopal’s testimony on this point was as follows:

JUDGE WALSH: All right. Passing on to Karen Brailsford.

Did you examine her echocardiogram to determine whether it was conducted in a technically adequate manner so that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it?

THE WITNESS: In this case, as well, I felt that it was not conducted in a technically adequate manner. The color gain was excessive in the parasternal long axis view. There was a lot of speckling, and that might have erroneously increased the apparent severity of aortic regurgitation.

JUDGE WALSH: All right. There was no mitral regurgitation claim made, but there was an aortic regurgitation claim made.

Did you examine the parasternal long axis view to determine whether it was available?

THE WITNESS: Yes. The parasternal long axis view was available and -- it was available.

JUDGE WALSH: All right. And did you make a judgment whether the parasternal long axis views showed FDA-positive aortic regurgitation by color flow Doppler?

THE WITNESS: I felt that the parasternal long axis view did show a consistent diastolic jet. However, in this case, I felt that the color gain was so excessive that it actually might have influenced the measured jet height. And, so, I didn't feel that it was reasonable to call this an FDA-positive case.

JUDGE WALSH: And, nevertheless, you measured it and found relative JH/LVOT measurement of one unit versus 14 units yielding, again, a percentage of about 7.14 percent. Is that correct?

THE WITNESS: That's correct.

JUDGE WALSH: All right. And I think you made the observation that the FDA-positive criteria aren't met even accounting for very high color gain noted in the PLAX view?

THE WITNESS: That's correct.

JUDGE WALSH: All right. Could a medical person with your skill sets acting in a medically reasonable way diagnose this patient with FDA-positive aortic regurgitation in the parasternal long axis view?

THE WITNESS: In this case I felt that another physician of similar training could reasonably disagree and call this an FDA-positive positive case because the jet was more than just a fleeting jet. And it's possible that the severity of the aortic regurgitation might have been overestimated by the gain.

So while I might not feel that the FDA-positive criteria were met, it's possible that another physician could see the situation otherwise.

JUDGE WALSH: Well, is it possible that another physician with your skill sets acting reasonably could determine that this echocardiogram was conducted in a

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technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it?

THE WITNESS: I mean, this goes to the question of whether the judgment was that the color gain was so excessive that you couldn't really make -- in other words --

JUDGE WALSH: That you couldn't make a quantitative conclusion?

THE WITNESS: Right.

JUDGE WALSH: So what's the answer?

THE WITNESS: Once again, I mean, I feel in this particular case that somebody could call this mild aortic regurgitation simply because of the fact that the jet was consistent. You know, it wasn't fleeting. It occurred in more than one or two diastolic frames. And, you know, the jet height ratio is pretty close to 10 percent. So, I mean, I think it's all the risk criteria that I found that I think that somebody else could have disagreed.

JUDGE WALSH: Well, again, I hear what you said about the -- about the actual diagnosis. The question is: Was the methodology such that a reasonable physician could disagree as to whether reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it? In other words, could any reasonable physician conclude that this echocardiogram was conducted in a technically adequate manner?

Do you have a problem?

MR. BLAIR: No, sir.

THE WITNESS: Well, you know, the thing is that in terms of the -- if the instructions were to simply -- you know, if the answer to question number one was no, then everything else, you know -- if the instructions were, well, then disregard everything else, don't make any measurements, then I would say somebody else might, you know -- might say, well, since the color was inadequate, you can't make any other statements and that's the case.

But I know in the past we felt that the color gain was high and we nevertheless -- and in this particular case, I actually did make some measurements. And, so, it's really taking the totality of experience and so forth in coming to that conclusion.

So while, again, I think while I might feel that it's not reasonable, I think another physician -- it's possible that it's within the realms of interobserver variability.

JUDGE WALSH: All right. I have to make two findings. The first one is this: Was the echocardiogram conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn? That's the first conclusion that I have to make based on all of the evidence, including your testimony.

The second is if this echocardiogram is technically adequate, then are the findings that you make FDA-positive? And a collateral finding that has to be made is if you find that it's not, could a reasonable physician acting with your skill sets conclude otherwise?

So, let's take the three questions. I don't care what the answers are. But what I need to know is could a reasonable physician with your skill sets acting reasonably conclude that this echocardiogram was conducted in a technically adequate manner such that reliable medical conclusions could be drawn from it?

THE WITNESS: I think another physician might -- might reasonably have felt that the color gain was sufficiently adequate to call this mild aortic regurgitation. And then, therefore, fulfill the FDA-positive criteria.

Reviewing this testimony in a light most favorable to Brailsford, the Court does not believe that a reasonable physician could conclude either that this echocardiogram was technically adequate or that it demonstrated MAR.

result of these observations, Dr. Gopal found that it was not reasonable to diagnose Brailsford with FDA positive aortic regurgitation ( $JH/LVOT \geq 10\%$ ) in the parasternal long axis view or, if the parasternal long axis view was unavailable, in the apical long axis view. She repeated her reasons for that determination, finding that “[c]olor gain was excessive, thus precluding accurate assessment of the jet height ratio necessary for determining FDA positivity.” Dr. Chen concurred.

While Dr. Mancina disagreed, the Court gives his testimony little weight since the gain of 15 significantly exceeded the maximum gain of 11 he had given his echocardiographers.

For these reasons, the Court finds that Wyeth has demonstrated that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it.

#### **Q. LADAUN G. BRENCHELEY**

Brenchley relies on a November 18, 2002 echocardiogram and report by Dr. Stanley S. Schrem. Dr. Schrem found Brenchley had MAR using CAS criteria --  $JH/LVOT = 19\%$ . The quality of the echocardiogram was listed as “fair.”

The November 18, 2002 report was reviewed by three (3) experts: Dr. Vasey, Dr. Gopal and Dr. Mancina. Dr. Vasey determined that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. He found “[t]he color Doppler gain was exceedingly excessive, making it difficult to make an accurate assessment of the presence and severity of regurgitation, if any.”

The gain setting here was 16, far above that which Dr. Mancina directed his echocardiographers to use. Nevertheless, Dr. Mancina believed that the echocardiogram could be used diagnostically. Dr. Gopal concurred.<sup>12</sup>

However, both Drs. Gopal and Vasey agreed that there was no evidence of MAR in the PLAX view. Dr. Vasey noted that “[e]ven with the high color Doppler gain, continuous wave Doppler through the five-chamber LVOT, shows

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<sup>12</sup> The excessive gain was compounded by the marginal Nyquist limit of 51 cm/sec. As Dr. Mancina acknowledged, the probe depth was 13.5 centimeters. Thus, a Nyquist above 70 cm/sec was possible.

no aortic insufficiency signal. Additionally, in the three-chamber apical view (loop 46), no aortic insufficiency signal is visualized by color flow mapping.” Dr. Gopal agreed, stating “[t]he jet was transient (lasted less than 2 videoframes) in the parasternal long axis view and was barely even visible on the apical view. It is hence consistent with trace aortic regurgitation. Dr. Mancina mentions images 28 and 33 which are images showing tricuspid regurgitation and mitral regurgitation respectively.”

Dr. Mancina claimed that MAR was present in the PLAX view. He measured a JH of .32 centimeters and an LVOT of 2.25 centimeters which computes to 14.2%. These measurements were made in a different location than those reported in his original affidavit.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner and hence no reliable medical conclusions can be based on it. In any case, Wyeth has also established that no reasonable physician could find MAR based on review of this echocardiogram.

## **R. SYLVIA BUNKALL**

Bunkall relies on a May 30, 2002 echocardiogram and report by Dr. Steven A. Rokeach. Dr. Rokeach found Bunkall had MAR. No indication exists in the report that CAS criteria were used nor are there any JH and/or LVOT measurements. Dr. Rokeach characterized the echocardiogram as a “technically fair study.”

The May 30, 2002 echocardiogram was reviewed by three (3) experts: Dr. Schwartz, Dr. Gopal and Dr. Mancina. All three (3) physicians determined that the echocardiogram was technically adequate.

Both Drs. Gopal and Schwartz found no evidence of aortic regurgitation in the PLAX view. Dr. Schwartz observed that “the images of parasternal long-axis view, which are of good quality, demonstrate that there is no aortic insufficiency present.” Dr. Gopal concurred.

Dr. Mancina did not disagree that the PLAX view was of good quality and was available. Instead, he took his JH and LVOT measurements in the apical 3 chamber view and reported a JH of .42 centimeters and an LVOT of 2.23 centimeters yielding 18.8%. The Court accepts Dr. Gopal’s criticism of that procedure.

The parasternal long axis view did not reveal any aortic regurgitation. Only trivial fleeting aortic regurgitation was noted on the parasternal short axis and apical views. The qualifying echocardiogram provides no specific jet height ratio measurements.

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There was no videoframes available even in the apical views in which the jet was clearly visualized at its origin. The videoframes provided only visualized portions of the jet more distal from the valve orifice, thus making jet height ratios inaccurate.

Dr. Mancina attempted to impeach the quality of Bunkall's echocardiogram in the PLAX view. An excerpt of that testimony follows:

THE WITNESS: Judge, this is -- this is -- falls in that category of 5 to 10 percent of people who are technically limited studies and sometimes it's body habitus. Sometimes it's lung disease. Sometimes a combination. And those are the most common things that we see that cause this.

JUDGE WALSH: You didn't call this a technically marginal study. You said everything was fine. Isn't that what you said in your certification?

THE WITNESS: No, I said that I had to use the Apical 3 chamber view because I couldn't access the information due to the technical quality of this study.

BY MR. WHEELER:

Q. Dr. Mancina, Ms. Carter questioned you this morning and asked you whether this was a technically adequate study and my recollection, the record will speak for itself, you said that it was. Do you recall that?

JUDGE WALSH: He sure did.

A. Well, not in this view. I said that -- I said that we have a composite of views that we can use and that we can make statements about the heart, even though the study may be limited in some views and other views is -- there's enough to make the diagnosis and that's just every day echocardiography.

Yet, on direct examination, Dr. Mancina unequivocally stated that the study was technically adequate.

Q. Let's move on to Ms. Bunkall. Did you review the echocardiogram of Ms. Bunkall?

A. Yes.

Q. Did you find it to be technically adequate?

A. Yes.

Q. Did you diagnose Ms. Bunkall with FDA-positive regurgitation?

A. Yes.

Q. Did you make measurements of the outflow tract and the regurgitant jet as seen on the echocardiogram?

A. I did.

Q. And what were your findings?

A. I found that 18.8 percent of the outflow tract was occupied by regurgitant flow during diastole.

The Court finds that Wyeth established that the PLAX view was available and demonstrated no aortic regurgitation. Moreover, the Court believes that any jet found in the apical views was too distal from the valve orifice, making any measurements unreliable. Accordingly, no reasonable physician could conclude on the basis of this echocardiogram that Bunkall has MAR.

## **S. ROCHELLE CALL**

Call relies on a June 2, 2002 echocardiogram and report of Dr. John E. Lassetter. Dr. Lassetter found Call had MAR using CAS criteria -- JH/LVOT = 14%.

The June 2, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Gopal and Dr. Mancina. Both Drs. Gopal and Goldman noted the high color gain. Dr. Goldman observed that in addition the Nyquist limit was at a marginal 51 cm/sec. And this was despite the interrogation depth of the probe being set at 10.8 centimeters. This would have allowed a Nyquist above 80 cm/sec. Nevertheless, both Drs. Gopal and Goldman felt the echocardiogram could be assessed.

Both Drs. Gopal and Goldman found that any jet observed in the PLAX view was “transient” lasting only “1 or 2 videoframes.” The jet plainly was not holodiastolic.

Dr. Mancina found this echocardiogram was technically adequate though his own testimony makes it clear that the quality was marginal.

Q. Let’s see Page 5 in real-time, please. Doctor, others have commented on the gain on this study. I wonder if you agree that it’s excessive?

A. The gain is 17.

Q. Yes, sir, that’s outside your range, correct?

A. It’s outside the range that we would normally like to use.

Q. And this is a study at 10.8 sonometers maximum depth with a Nyquist limit at 51.

A. Correct.

Q. The Nyquist certainly could have been higher, above 60, perhaps above 70?

A. That’s correct.

JUDGE WALSH: Could have easily been above 70.

THE WITNESS: That’s correct.

While Dr. Mancina claims to have measured a JH of .24 centimeters and an LVOT of 1.96 centimeters, implying a JH/LVOT of 12.2%, a review by the Court of the media indicates that the jet is present only in one (1) or two (2) frames.

The Court finds that Wyeth has established that no reasonable physician could diagnose MAR based on a review of this echocardiogram. This marginal quality echocardiogram simply fails to show anything approaching a holodiastolic aortic jet.

## **T. JAYNE CHATTERTON**

Chatterton relies on a June 29, 2002 echocardiogram and report by Dr. Scott L. Roth. Dr. Roth found Chatterton had MAR using CAS criteria -- JH/LVOT = 20%. Dr. Roth noted that this was a “technically adequate study.” The sonographer noted “technically difficult apical views.”

The June 29, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Gopal and Dr. Mancina. Both Drs. Gopal and Goldman found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Both physicians noted that the gain was high and Dr. Goldman also noted the marginal Nyquist limit of 51 cm/sec. Dr. Mancina claimed that the echocardiogram was technically adequate but the gain was set at 19, well beyond the settings he directed his sonographers to use.

Both Drs. Goldman and Gopal concluded that review of the echocardiogram, despite its technical limits, led to a conclusion that no MAR was present. Dr. Goldman noted that “[d]espite being acquired with poor technique, no sustained holodiastolic turbulent jet of aortic insufficiency is present. Additionally, continuous wave Doppler (loop 38) shows no aortic insufficiency.”

Dr. Gopal was of the same view, observing that “[c]olor gain was higher than desirable and so would have biased the study in favor of FDA positive aortic regurgitation. Even assuming that the color gain is adequate, FDA positive criteria are not reached.” Accordingly, she found that no reasonable medical conclusion that Chatterton has MAR could be drawn from review of this echocardiogram.<sup>13</sup>

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<sup>13</sup> The Court is aware that Dr. Gopal was equivocal on this question at the hearing. So that the reader can get the context of her testimony, the direct examination is set out in full.

JUDGE WALSH: All right, then. We'll pass to Chatterton, Jane Chatterton.

Was this echocardiogram conducted in a technically adequate manner such that a lot of the medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it?

THE WITNESS: No. This study had excessive color gain in the parasternal long axis view. There were many speckled regions. And, so, I didn't feel that it was conducted in a technically adequate manner.

JUDGE WALSH: There was no mitral regurgitation claim made. There was an aortic regurgitation claim made.

Was the parasternal long axis view available on this echocardiogram?

THE WITNESS: Yes, the parasternal long axis view was available.

JUDGE WALSH: And does the parasternal long axis view show FDA-positive regurgitation by color flow Doppler for this particular individual?

THE WITNESS: I felt here that the color gain was higher than desirable and may have overestimated the aortic regurgitation jet height. So, even assuming that the color gain is adequate, I actually made some measurements of my own suggesting that the jet height ratio was less than 10 percent, and, therefore, not qualifying for FDA positivity.

JUDGE WALSH: All right. You actually made a measurement at the parasternal long axis view, I guess image number seven, it appears, and you found two millimeters over 21.1 millimeters, which you calculated to 9.5 percent.

JUDGE WALSH: That's correct.

JUDGE WALSH: And you noted FDA-positive criteria are not strictly met.

Dr. Mancina found otherwise. He concluded that Chatterton has MAR with a JH/LVOT of 14.6%. This was based on his measurement of a JH of .31 centimeters and an LVOT of 2.12 centimeters. Cross-examination of Dr. Mancina illustrates the poor echocardiogram quality as well as the tenuous nature of his measurements.<sup>14</sup>

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THE WITNESS: That's correct.

JUDGE WALSH: Could a physician acting reasonably diagnose this patient with FDA-positive aortic regurgitation in the parasternal long axis view based on this echocardiogram using standards set forth by me to you in a letter?

THE WITNESS: I felt in this case that another physician could have called this mild aortic regurgitation using the standards set forth by the Court.

JUDGE WALSH: All right. Let's go back to question number one. Could a physician acting reasonably conclude that this echocardiogram was conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it?

THE WITNESS: I think, once again, the issue of color gain and whether you can sort of ignore that is the question at hand right now. In my case, I kind of used a conservative estimate of the jet height ratio because I felt that the color gain was higher than desirable, but another physician might have concluded differently.

And I felt that the jet height ratio that I computed, 9.5, is pretty close to ten. And, so, I felt that this is, again, within that realm of interobserver variability.

And there was a consistent color flow jet. And I guess I put the consistency, the fact that it was consistent and not a transient jet, as, you know, as being more indicative of mild aortic regurgitation. And that's why I felt that, you know, this was -- this could have been interpreted by another physician as mild aortic regurgitation. I think that's reasonable.

JUDGE WALSH: All right. Why did you answer -- when the question was asked: Is it medically reasonable to diagnose this plaintiff with FDA-positive aortic regurgitation in the parasternal long axis view based on this echocardiogram using the standards set forth by the Court? you answered no. That's number eight.

THE WITNESS: Yeah. I answered no because, number one, the color gain was excessive; and, secondly, even assuming the color gain was excessive, I conducted some measurements which fell below the limits set forth by the Court.

And, so, giving all the benefit of the doubt to the patient, I felt that this was not reasonable to call this mild aortic regurgitation, but it's in that borderline category. So I felt that somebody else could have reasonably concluded that this was mild AI.

<sup>14</sup> Dr. Mancina's cross-examination follows:

Dr. Mancina, wouldn't you agree with me that the Nyquist limit of 51 at a depth of 16.2 centimeters could have and should have been higher in excess of 60?

A. It could have been.

Q. And wouldn't you agree with me that you actually traced in this image something distal from the valve orifice that is within the color map of a 51 Nyquist limit evidencing low flow blood, low velocity flow? I'm sorry.

A. It's relatively low velocity flow here, all right, but there are some elements in it that looked like higher velocity.

Q. And you would agree --

The Court finds that Wyeth has established that the echocardiogram here was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The echocardiogram was plainly overgained. But leaving this aside, Wyeth has established that CW Doppler demonstrates no holodiastolic jet. The Court finds that no reasonable physician could find that Chatterton has MAR by examination of this echocardiogram.

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A. So this is just a frame, I have to see the whole jet to be a little bit more specific.

Q. Yes, sir. I'm just simply looking at the frame that you referenced.

A. Sure.

Q. And you would agree with me, would you not, Doctor, that there is color speckling into the tissue?

A. There's color override of the tissue, I don't know if that's speckling. I would have to look real-time, I think.

Q. Let's do that then, let's look at Page 4 in real-time then, T.J.

Would you not agree, Dr. Mancina, that this is color speckling in the tissue in real-time on this particular page that you relied upon?

A. Yes, there is.

Q. Go to Frame 31, please, T.J.

This is the image I believe that you actually made your measurements on, Dr. Mancina, is that right?

A. It looks like the way we were just seeing in freeze frame.

Q. At what stage of diastole are we electrically, Doctor?

A. I think we're behind the Access Point measure. It looks like it's early to mid diastole.

Q. All right. Let's go forward. Actually, let's go backward if it's early. Go back to Frame 40. Now, go forward, T.J., 31, 32, 33. By 33, Doctor, do you see any evidence --

A. Yeah, I still see evidence. Keep going. Yes. Yes.

Q. 36?

A. Yes.

Q. 37?

A. We're, essentially, through diastole there.

Q. And the images that you saw, Doctor, were all within the color map, were they not, consistent with the image that you traced?

A. I'm not sure I understand your question.

Are you saying that what I was seeing was part of a jet in each of these frames.

Q. What you believed to be a jet, would you agree that the color of that image was within the color map?

A. Oh, yes.

Q. Thank you. And that color map was for a Nyquist of 51?

A. Correct.

## U. ERMA L. CONOVER

Conover relies on a July 10, 2002 echocardiogram and report of Dr. Charles F. Dahl. Dr. Dahl found that Conover had MAR using CAS criteria -- JH/LVOT = 12%. The sonographer found moderate aortic regurgitation ("MMAR").

The July 10, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. Both Drs. Millman and Goldman found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Millman concluded that "[t]here is excessive gain in the color [D]oppler producing considerable signal noise, and the Nyquist limit is set too low at 41 cm/sec." Dr. Goldman concurred.

Dr. Mancina disagreed but, as noted throughout this Letter Opinion, the gain setting was 15, well above the directions given to his sonographers for the proper conduct of echocardiograms.<sup>15</sup> Not only was the Nyquist set at a ridiculously low

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<sup>15</sup> Dr. Mancina was almost apologetic in defense of this poorly acquired echocardiogram.

Your Honor, this is a DICOM study at D-6045. You relied on, I believe Page 6, Frame 35, is that right, Doctor?

A. Yes.

Q. If we could look at that frame, T.J., Page 6, Frame 35, please. Doctor, what's the Nyquist limit on this study?

A. 41.

Q. What's the maximum depth being imaged?

A. 13.5 centimeters.

Q. Wouldn't you agree, Doctor, that there is no scientific explanation for why a sonographer would utilize a Nyquist limit of 41 when imaging a depth at 13 and a half centimeters?

A. We would ordinarily advise our sonographers to try to achieve a higher Nyquist.

Q. And certainly that would have been achievable here at a maximal depth of 13 and a half centimeters, correct?

A. Most likely.

Q. Well, Doctor, that's a bit of a hedge; it's not most likely, that would be definitively, wouldn't it?

A. Most likely.

Q. Fair enough, Dr. Mancina?

JUDGE WALSH: Doctor, listen --

THE WITNESS: Theoretically, based on 13.5 centimeters, you should be able to obtain a higher Nyquist.

JUDGE WALSH: You have seen on this Cypress machine repeatedly color velocities of at least 61 centimeters per second were achievable at 13.5 centimeters of depth.

I mean, wouldn't you allow that imaging at a -- you'd agree that 41 centimeters per second is a really low Nyquist limit, wouldn't you?

A. It's one we don't use generally.

41 cm/sec, but it is clear from the probe depth that it could have been set at over 70 cm/sec.<sup>16</sup>

The Court finds that Wyeth has easily satisfied its burden to show that this echocardiogram was not conducted in a technically adequate manner and virtually no useful information can be obtained from its review.

## V. CAROL G. COULAM

Coulam relies on a July 8, 2002 echocardiogram and report by Dr. Arthur Schwartzbard. Dr. Schwartzbard found Coulam had MAR using CAS criteria -- JH/LVOT = 15%. The quality of the echocardiogram was listed as “fair.”

The July 8, 2002 echocardiogram was reviewed by three (3) experts: Dr. Schwartz, Dr. Millman and Dr. Mancina. Both Drs. Millman and Schwartz determined that the echocardiogram was not technically adequate such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Millman succinctly reported that “[t]he color [D]oppler gains are set so high as to make a meaningful [D]oppler signal non-retrievable.” Dr. Schwartz concurred. Because the echocardiogram lacked any technical adequacy, neither physician even attempted to identify an aortic jet. Review of the CW Doppler revealed none.

Dr. Mancina disagreed. Though it was clear that the gain setting of 18 greatly exceeded the maximum gain setting permitted his sonographers, Dr. Mancina insisted that this echocardiogram was of adequate technical quality.<sup>17</sup> Dr.

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JUDGE WALSH: I think that's fair to say.

THE WITNESS: Not at 13.5 centimeters, we wouldn't.

JUDGE WALSH: It's inexplicable how some sonographers -- no sonographers that you trained would do this, am I correct?

A. I would expect they wouldn't do this.

<sup>16</sup> Dr. Thomas noted that for Conover

with purported mild aortic regurgitation (12%), the Nyquist limit was set at 41 cm/sec despite a depth of 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec), and aortic regurgitation could have been imaged at 10.8 cm (theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit was set at 41 cm/sec despite a depth of 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec).

<sup>17</sup> Dr. Mancina conceded the high gain in the PLAX view.

Q. You agree, do you not, Dr. Mancina, that the parasternal long axis view is available on this study, at least at a couple of different pages of the DICOM echo?

A. I chose the Apical 3 chamber. I'd like to see the parasternal long axis to see why, right, sir.

Mancina could not measure any regurgitant jet in the PLAX view and then proceeded to measure JH and LVOT in the apical long axis view. He found a JH of .36 centimeters and an LVOT of 2.16 centimeters which computes to 16.7%.

The Court finds that Wyeth easily has demonstrated that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it.

## **W. ROBERT COWGILL**

Cowgill relies on a July 11, 2002 echocardiogram and report of Dr. Scott L. Roth. Dr. Roth found Cowgill had MAR using CAS criteria -- JH/LVOT = 15%. The sonographer noted that she could not evaluate Cowgill in the PLAX or apical views.

The July 11, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. Both Drs. Millman and Goldman found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Millman's remarks best encapsulate these physicians' opinions. "The color [D]oppler gains are set too high to record meaningful data. In addition, the Nyquist limit is set to[o] low at 46 cm/sec."<sup>18</sup>

Dr. Mancina found this echocardiogram to be technically adequate although gain settings here were 17, well above his cutoff of 11. Despite his claim that this

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Q. Let's look at Page 11 of this study. I suppose one preliminary comment would be, Doctor, that the gain is rather excessive in this study. I think it's quantified at 18 and is exhibited by significant speckling into the tissue. Do you agree?

A. Yes.

Q. This is, however, a parasternal long axis view that was available to you and the interpreting physician originally with respect to this study?

A. Yes.

<sup>18</sup> Dr. Thomas noted that for Robert Cowgill,

with purported aortic regurgitation (15%) claimed from apical long axis window despite acceptable parasternal long-axis images, the Nyquist limit was set at 46 cm/sec (the Cypress maximal Nyquist limit for depth of 21.7 cm). However, the LVOT could have been visualized at 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit was set at 46 cm/sec (maximum for depth of 21.7 cm) but the mitral valve and left atrium could have been visualized at a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec).

was a technically adequate echocardiogram, Dr. Mancina could not document the aortic regurgitation in either the PLAX or apical long axis views. His testimony in this respect is clear.

Q. Let's move to Robert Cowgill. Did you review the echocardiogram of Mr. Cowgill?

A. Yes.

Q. Did you find it to be technically adequate?

A. Yes.

Q. Did you diagnose this patient with FDA-positive regurgitation?

A. Yes.

Q. And it was my understanding that you were unable to make measurements of the jet and outflow tract in the PLAX or Apical 3 view, but is it your opinion based upon your experience, education, and training as a cardiologist that Mr. Cowgill has FDA-positive regurgitation?

A. Yes.

The Court finds that Wyeth easily established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. In any case, there was no evidence offered by the plaintiff, other than a net opinion, that Cowgill has MAR using the CAS criteria.

## **X. LISA CREBS**

Crebs relies on a November 20, 2002 echocardiogram and report of Dr. Robin S. Freedberg. Dr. Freedberg found Crebs had MAR using CAS criteria -- JH/LVOT = 22%. The sonographer reported MMAR with a JH/LVOT = 31%. The quality of the echocardiogram was listed as "good."

The November 20, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. Both Drs. Millman and Goldman found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Millman observed that "[t]he color [D]oppler gain controls are set very high precluding any meaningful color [D]oppler analysis of any purported aortic regurgitation." Dr. Goldman concurred.

Dr. Mancina disagreed that the echocardiogram was technically inadequate but had to acknowledge that the gain of 14 exceeding the maximum gain reported in his memoranda. Dr. Mancina reported a JH of .52 centimeters and an LVOT of 2.24 centimeters which computes to 23.2%.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The color gain settings were simply too high to derive any meaningful information from this echocardiogram.

## **Y. DELILAH DAVIS**

Davis relies on a November 11, 2002 echocardiogram and report by Dr. Charles F. Dahl. Dr. Dahl found Davis had MAR using CAS criteria -- JH/LVOT = 22%. The sonographer noted “[d]ifficult ranges due to COPD.”

The November 11, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate.

Both Drs. Mancina and Millman found Davis has MMR. Dr. Mancina measured a JH of .31 centimeters and an LVOT of 2.01 centimeters, implying a JH/LVOT = 15.4%, but his measurement was taken in the apical long axis view.<sup>19</sup> Dr. Millman measured a JH/LVOT = 10% in the PLAX view. Dr. Goldman saw no sustained jet in the PLAX and believed that CW Doppler indicated “no signal or aortic insufficiency.”

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<sup>19</sup> Dr. Mancina had no adequate explanation for his action here.

Q. You would agree, would you not, that the PLAX view was available on this study?

A. I didn't use the PLAX view.

Q. My question is not whether you used it, Doctor, but whether it was available to you on the study?

A. My understanding of available was that it was a view in which we could interpret and measure a jet and I couldn't in this patient. That's why I used the Apical 3 chamber, which was the other alternative.

Q. Let's look at Page 58, the view --

JUDGE WALSH: This is following the directions from the Williams Bailey firm?

THE WITNESS: Well, I believe the matrix says that if you can't measure in the parasternal long axis, the other available view is Apical 3 chamber.

The Court finds that Wyeth has failed to establish that no reasonable medical conclusions that Davis has MAR could be drawn from this echocardiogram. As Dr. Millman noted, the quality of some of the views is “dreadful.” Moreover, Dr. Mancina did not use the PLAX view to quantify the MAR although it plainly was available. Finally, Dr. Goldman’s observation that the jet is not documented on CW Doppler is true though the CW Doppler angle may partially explain this. Despite these flaws, the Court believes that a reasonable medical opinion that Davis has MAR could be drawn from this echocardiogram.

## **Z. MARCIA DeWITTE**

DeWitte relies on a September 16, 2002 echocardiogram and report of Dr. Robin S. Freedberg. Dr. Freedberg found DeWitte had MAR using CAS criteria --  $JH/LVOT = 14\%$ . The sonographer noted a higher  $JH/LVOT$  of 21%. The quality of the echocardiogram was listed as “good.”

The September 16, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate.

Both Drs. Millman and Mancina found DeWitte has MAR. Dr. Millman measured a JH of 2.2 millimeters and an LVOT of 20 millimeters which implies 11%. Dr. Mancina measured a JH of .3 centimeters and an LVOT of 1.73 centimeters, implying a  $JH/LVOT = 17.3\%$ .

Dr. Goldman disagreed, finding that there was “no sustained holodiastolic jet of aortic insufficiency....” He believed his opinion was supported by CW Doppler.

The Court finds that Wyeth has failed to satisfy its burden to show that no reasonable medical conclusion that DeWitte has MAR could be made based on review of this echocardiogram.

## **AA. DANIELLE EYRE**

Eyre relies on a November 14, 2002 echocardiogram and report of Dr. John E. Lassetter. Dr. Lassetter found that Eyre had mild mitral regurgitation but apparently found no aortic regurgitation. The sonographer wrote “[n]o AI.” The quality of the echocardiogram was listed as “fair.”

The November 14, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. All three (3) physicians found that the echocardiogram was technically adequate.

Both Drs. Millman and Goldman found no significant aortic regurgitation. Dr. Goldman noted that “[n]o sustained holodiastolic turbulent jet of aortic insufficiency is present. Continuous wave Doppler (loop 37) shows no sustained jet of aortic insufficiency. Additionally, the original sonographer’s worksheet states ‘no aortic insufficiency.’” Dr. Millman simply noted “no significant aortic regurgitation.”

Dr. Mancina reported that Eyre has MAR based on a JH of .42 centimeters and an LVOT of 2.0 centimeters, implying a JH/LVOT = 21%. However, during the hearings, Dr. Mancina initially could not find the frame where he made his measurement. After a break, he identified it. It was clear to the Court that this jet lasted for only a couple of frames and CW Doppler made it clear that this was not a holodiastolic jet.<sup>20</sup> The Court also questions the JH measurement as it was not measured properly and should be significantly smaller.

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<sup>20</sup> Dr. Mancina argued about the CW Doppler findings in his testimony.

Q. Page 37, please.

Doctor, I'm showing you what is the continuous wave reportedly of aortic regurgitation.

Does it or does it not appear that there's nothing there that would be suggestive of certainly high velocity, much less an envelope?

A. Well, I would say that this is -- there are signals in diastole. If you look at the frame that is the very first of the diastolic frames, which precede the first R wave. And if I can point it out to you what I'm referring to.

I think you ought to look at the monitor to see this because you're going to have a hard time seeing it on

this screen, but here is the R wave. The first R wave is here. So, the first diastolic period is in here. If you go to either a different representation of the activity here in terms of signals, like changing the color, you will see this light up a bit better. And now you can see some red cells in here. The red cells are moving in diastole, and they follow systole.

JUDGE WALSH: I have a lot of problems with this one. I mean, that looks to me like it's just background that exists in any CW. There's no real indication of any jet here, but -- and these jets are one meter, I mean, which is really very unimpressive.

THE WITNESS: I'm not going to try to impress you with this particular frame, but I look at the whole study. I don't look at one frame as you fellows do.

JUDGE WALSH: Listen, Doctor, we're here to learn. I'm here to look at every CW shot there is here. You're the one who told us to go to CW, so that's where we are. I'm looking at it. It tells me that in diastole, you see nothing really approaching an envelope. And you don't see velocities above one meter. I mean -- you know, it's really very telling.

The Court finds that Wyeth has satisfied its burden and has demonstrated that no reasonable physician could find that Eyre has MAR through review of this echocardiogram. Moreover, the Court even questions whether Eyre should have been permitted to opt-out in the first place based on an echocardiogram report which indicates that she does not have FDA positive aortic regurgitation.

## **BB. JUDY M. FIELDING**

Fielding relies on a September 17, 2002 echocardiogram and report of Dr. Edward S. Katz. Dr. Katz found Fielding had MAR using CAS criteria -- JH/LVOT = 20%. The sonographer had noted JH/LVOT ratios somewhat higher at approximately 30%. The quality of the echocardiogram was listed as "fair."

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THE WITNESS: Well, let me say this. I don't think we have a very good representation of what's going on here. And if you might, or if you'd like to, we can go through more of the study to try to delineate whether this person has aortic valve regurgitation.

JUDGE WALSH: Let's look the at CW. Is this is the only CW here?

MR. RAMSAY: I think so. It's the only one that I'm aware of.

JUDGE WALSH: If it is, we went where you wanted to go, and it is underwhelming.

Q. Doctor, in any event, rather than prolong it, based upon the frame that you selected, we can agree that at least with the color [D]oppler, there is no suggestion or indication of holodiastolic flow? And I realize your reservations about that technique, but it did not show holodiastolic flow; did it?

A. We didn't have a holodiastolic flow except in a few frames, but that is very common.

Q. Yes, sir.

And here, again, then we looked at CW and there was no confirmatory evidence holodiastole as far as a regurgitant jet in the CW; was there?

A. It shows you the limitations of these techniques.

Q. Yes, sir.

JUDGE WALSH: There was certainly no indication of an aortic jet here; is that true?

THE WITNESS: No, I disagree with that. I think that there are red cells, and I think that it's greater than 2 meters, and I think that's AI. However, if you look at the continuous wave line, you see in the small --

JUDGE WALSH: Yes, in the small --

THE WITNESS: -- screen above, you'll see this technician is off axis.

JUDGE WALSH: Well, okay.

THE WITNESS: And so you can miss it. And I'm just telling you that we have to look at all views, and sometimes jets are missed.

Q. Yes, sir.

A. So, I'm not willing to concede that this is not showing us AI. And I think that there is red cell in diastole that's being -- giving us signals, and the signals show that the velocity is greater than 2 meters.

JUDGE WALSH: I'm sitting here, and it's perfectly clear to me that there is nothing approaching 2 meters in any of this CW. And that's going to be my finding.

The September 17, 2002 echocardiogram was reviewed by three (3) experts: Dr. Goldman, Dr. Millman and Dr. Mancina. Both Drs. Millman and Goldman found that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Millman observed that “[t]he color gains were set very high, and although the Nyquist limit is appropriate, 51 cm/sec, there is no meaningful data obtainable, the one area at the end of the study where the [PLAX] is repeated shows only the closing artifact of the aortic valve, not aortic regurgitation.” Dr. Goldman concurred.

Dr. Mancina concluded that the echocardiogram was technically adequate despite a gain setting of 12. He found that Fielding has MAR finding a JH of .26 centimeters and an LVOT of 2.15 centimeters, yielding 12.1%. But he conceded that CW Doppler and color Doppler failed to confirm a holodiastolic jet.<sup>21</sup>

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<sup>21</sup> Dr. Mancina’s testimony in that regard is produced below.

Q. You talked about the gain. Do you see any evidence of a holodiastolic jet in all of page 44, sir? You don't; do you?

A. No, I don't see a holodiastolic jet, but I don't expect to have to see a holodiastolic jet in this view.

Q. Well, if not in the PLAX view, in what view would you expect to see a holodiastolic jet, or do you ever expect to see a holodiastolic jet on color [D]oppler?

A. Well, we do sometimes see a holodiastolic jet on color [D]oppler. There's a problem with this, and we've been through this when you weren't here. And that is that we are -- we have a fixed transducer of the chest, and the heart is a shifting direction.

Q. And I realize it runs parallel, and it can within and without the view during the circle?

A. Correct. So, we may not be expect to see a holodiastolic jet in this view, but we use the whole echocardiogram.

Q. Yes, sir.

A. I don't look at one view.

Q. But my question to you is, do you see any regurgitation in page 4?

A. I believe I see some in page 4, but it's not very much.

Q. Yes, sir.

If you go to page 22, which is continuous wave. Here again, I think according to your prior testimony, this is something you used for confirmation as to whether it, in fact, is truly a jet that lasts throughout all or most of the cycle; correct? Isn't that what you've testified before?

A. You mean about this particular patient?

Q. No, sir. The continuous wave is a tool that you utilize as confirmatory of whether or not what you see lasts throughout most all of the cycle?

A. Mr. Ramsay, I think you're misunderstanding what I said earlier. I said that we do use the continuous wave to try to judge whether somebody has holodiastolic, but that is not the only thing I use.

Q. All right. Are you suggesting to this Court that this particular continuous wave on page 22 confirms the existence of a holodiastolic high velocity jet?

The Court finds that Wyeth has satisfied its burden to show that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Moreover, Wyeth has established that a review of this technically flawed echocardiogram shows no evidence of holodiastolic aortic regurgitation.

## **CC. WALLACE J. HUNSAKER**

Hunsaker relies on a March 27, 2002 echocardiogram and a May 7, 2002 report of Dr. George C. Miller. Dr. Miller found Hunsaker had MAR using CAS criteria -- JH/LVOT = 19%.

The March 27, 2002 echocardiogram was reviewed by three (3) experts: Dr. Schwartz, Dr. Ong and Dr. Mancina. All three (3) physicians found that the echocardiogram was technically adequate.

Both Drs. Mancina and Ong determined that Hunsaker has MAR. Dr. Mancina made his measurements in the apical long axis view. He found a JH of .67 centimeters and an LVOT of 3.02 centimeters, yielding 22%. The LVOT here is so large that it is virtually certain that it is significantly overstated. Dr. Ong also made measurements in the apical long axis view and found a JH of .48 centimeters and a significantly smaller LVOT, yielding 18%. However, Dr. Ong found that the PLAX view was available and that it presented no technical difficulties.<sup>22</sup> Using the PLAX view, Dr. Ong saw no aortic regurgitation.

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A. No, I don't see that here.

<sup>22</sup> Dr. Ong's direct testimony on this point is produced in full.

JUDGE WALSH: All right. You had an opportunity to examine the echocardiogram of Wallace Hunsaker --

THE WITNESS: Yes.

JUDGE WALSH: -- to determine whether it was conducted in a technically adequate manner such that reliable medical conclusions regarding the severity and presence of valvular regurgitation could be drawn from it.

What did you find?

THE WITNESS: I found that it is valid. It is a technically adequate study.

JUDGE WALSH: All right. There was no mitral claim, but there was an aortic claim.

Was the parasternal long axis view available on this echocardiogram?

THE WITNESS: No.

JUDGE WALSH: All right. And when you answered "no," what did you mean by that?

THE WITNESS: I did not see any aortic regurgitation on that view. The view was present, but I did not see any.

Dr. Schwartz agreed with Dr. Ong that no aortic regurgitation was present in the PLAX view. Dr. Schwartz found that the PLAX view was adequately visualized and saw no regurgitation. He also criticized Dr. Mancina's LVOT measurement of 3.02 centimeters as "not possible."<sup>23</sup>

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JUDGE WALSH: All right. The general criteria is to look at the PLAX view first?

THE WITNESS: Yes.

JUDGE WALSH: In looking at it, did you find that there were any technical difficulties with parasternal long axis view?

THE WITNESS: No.

JUDGE WALSH: All right. You did look at the apical long axis view, and you basically made some findings based on that. Is that correct?

THE WITNESS: That's correct.

JUDGE WALSH: All right. Could you tell us what those findings were?

THE WITNESS: I noted several views in which a jet of aortic regurgitation was present, such as at time stamp 2:12:03, 2:15:35 and 2:16:50. The measurements in those views ranged from a ratio of jet height to LVOT ratio from .45 to .54, which is greater than 10 percent of the FDA criteria.

JUDGE WALSH: You measured one such frame and found the JH/LVOT was 18. Is that correct?

THE WITNESS: Yes.

JUDGE WALSH: All right. I'm going to ask you two questions on this to just make sure we have good order here.

First, could a reasonable physician with your skill sets conclude, based on views in the parasternal long axis view, that Mr. Hunsaker had at least mild aortic regurgitation by FDA criteria?

THE WITNESS: No, because I did not see anything in that view.

JUDGE WALSH: All right. Now, would it be medically reasonable, based on apical three or so-called apical long -- these were apical long axis views you had?

THE WITNESS: That's correct.

JUDGE WALSH: To conclude that this patient had FDA-positive aortic regurgitation by criteria?

THE WITNESS: Yes.

<sup>23</sup> Dr. Schwartz's testimony on these points is produced below.

Q. Wallace Hunsaker, it's a March 27, 2002 echocardiogram, Defense Exhibit 6058, another aortic claim.

Dr. Schwartz, what was your opinion with regard to the technical adequacy of this echo?

A. It was technically adequate.

Q. And was the parasternal long axis view available on this echo?

A. Yes, it was.

Q. Okay. I'm going to put the echo up here now and I think there's actually a couple places, so if you could just tell us where in the parasternal long axis with color and then we can fast forward in between.

A. Okay.

MS. PETERSEN: And T.J., you can probably just sort of fast forward it and then the doctor can stop it when we see.

A. This is the parasternal without color. This is a Hewlett Packer machine, okay. This is a zoomed-in color on the aortic valve area in the left ventricular outflow tract.

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Q. Okay. And do you see aortic regurgitation on this segment of the parasternal long axis?

A. Not here.

Q. Okay.

A. No, I don't, even going backwards, too.

Q. Let's go to the next spot where there's the parasternal long axis view.

MS. PETERSEN: Are we going forward?

THE TECHNICIAN: Yeah.

A. This continues to be parasternal long axis, again now. This is without the zoom. This is Color Doppler interrogation of the parasternal long axis.

Q. And reviewing this in real-time, do you see aortic regurgitation in the parasternal long axis view?

A. No.

Q. Okay.

A. This is still Color Doppler of the parasternal long axis.

Q. And I think that --

A. Same thing.

Q. There's no aortic regurgitation?

A. No, AI.

Q. And finally, if we can go forward to about 6:04, I think there's some more.

A. This is the parasternal short, L.V. outflow, left ventricular inflow, parasternal short, keep going. Now, this is the parasternal long again.

Q. And we'll wait for the color to start.

A. And this is Color Doppler on the parasternal long. I do not see AI here either.

Q. So in your opinion, reviewing all the parasternal long axis frames available, did you see any aortic regurgitation?

A. No, I don't.

Q. Okay. Let's look at the frame cited by Dr. Mancina and for the record, I'd just like to make clear that these are new time markers not previously disclosed until yesterday. JUDGE WALSH: Are they in a PLAX view?

MS. PETERSEN: No.

JUDGE WALSH: These are apical 3s.

MS. PETERSEN: Well, the jet height is in the apical, but the LVOT is in the PLAX.

JUDGE WALSH: Is that permissible?

THE WITNESS: I don't think you should measure the jet height on the apical 3.

JUDGE WALSH: Well, that I understand. Is there something -- I mean we're talking about, when we're doing the LVOT, we're talking about a two dimensional image; so I take it the PLAX would capture that two dimensional image in probably its best aspects?

THE WITNESS: I think that would be the best thing to do in that situation, to take the L.V. and the PLAX. Just as you'd want to get the best left atrial area that you can get in the study --

JUDGE WALSH: And the reason is because when you're imaging two dimensional -- when you're imaging two dimensions, cardiac structures, you want to be perpendicular as opposed to parallel?

A. Yes.

Q. Let's look first at the JH measurement from Dr. Mancina, which is Defense Exhibit 6252 at time marker 15:51:10, FTI 805045.

Dr. Schwartz, could you tell us what view this is in?

A. This is the apical three chamber.

Q. And was the --

JUDGE WALSH: Why is this so fuzzy?

MS. PETERSEN: I think this might be because it's a clip from the video.

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JUDGE WALSH: All right.

MS. PETERSEN: The video tapes are just more difficult to see. And was the parasternal long axis view available on this echo.

A. Yes, I think we showed that.

Q. Let's look at the LVOT measurement at the time marker 24:02. FTI 8042 and we've marked it Defense Exhibit 6253.

JUDGE WALSH: These are new countries heard from from the time stamps that Dr. Mancina initially revised -- I think initially he said 2:17:24, right?

MS. PETERSEN: That's right.

JUDGE WALSH: And 2:17:22.11.

MS. PETERSEN: Correct.

JUDGE WALSH: What are these new countries heard from?

MS. PETERSEN: 16:51:10 and 00:24:02.

JUDGE WALSH: These are all apical 3s, correct?

MS. PETERSEN: I'm sorry, go ahead.

JUDGE WALSH: These are apical 3s.

MS. PETERSEN: The news ones, the first was an apical and this is the parasternal, where the LVOT is.

JUDGE WALSH: Fair point. The 0:24:02 is the LVOT taken in the PLAX view?

MS. PETERSEN: Right.

JUDGE WALSH: All right.

Q. Dr. Schwartz, what LVOT measurement does Dr. Mancina get?

A. 3.02.

Q. And before looking at this image, would an LVOT measurement of that size cause you any pause?

JUDGE WALSH: That's pretty big, huh?

THE WITNESS: That does not seem realistic. That's not possible.

JUDGE WALSH: I guess Richard Perry couldn't qualify with a 3.02 LVOT.

THE WITNESS: It's not going to be physiologically likely.

JUDGE WALSH: It's not in the realm of possibility. I take it there's a standard way of looking at this. I guess 1.9 to 2.1 is probably within the general range where you'd probably see about 70 percent of your --

THE WITNESS: I think more. It's remarkable how it hovers around 2.0 very closely.

JUDGE WALSH: All right. So if you used a standard deviation analysis, and if you're telling me the variance is so close that one standard deviation is between plus and minus .1, what you're saying is this is not physically possible?

THE WITNESS: Well, no, it's not physically possibly, especially in the context of this echo which looks fairly normal. The reason they got such a big number is they're not measuring the L.V. outflow tract diameter. This is the partial measurement of the aortic root.

JUDGE WALSH: I guess what counsel, Mr. Blair, will say is "so what?" So it's implausible. He's giving you the benefit of the doubt by a long shot so --

THE WITNESS: I just think it shows --

JUDGE WALSH: It shows that he doesn't know what he's doing.

THE WITNESS: To me, it shows that the person wasn't competent to measure the measurements.

JUDGE WALSH: I get the picture.

EXAMINATION BY MS. PETERSEN:

Q. So in your opinion was this a medically reasonable measurement of LVOT?

A. It's not medically reasonable.

Q. And would it be medically reasonable to conclude that Mr. Hunsaker has FDA-positive aortic regurgitation?

A. No.

The Court finds that Wyeth has established that the PLAX view was available and technically adequate. Moreover, it is clear that a review of the PLAX views shows no aortic regurgitation. While apical long axis views may provide sufficient information to satisfy a clinician that Hunsaker has MAR, the CAS criteria are clear that the determination must be made in the PLAX view if available. It was available here.

## **DD. VICKIE A. HYMAS**

Hymas relies on a July 1, 2002 echocardiogram and report by Dr. Charles F. Dahl. Dr. Dahl found Hymas had MAR using CAS criteria -- JH/LVOT = 20%. The quality of the echocardiogram was listed as "fair."

The July 1, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Ong and Dr. Mancina. Both Drs. Ong and Stern concluded that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Stern noted that "[t]he color gain setting is too high, causing a very noisy picture with 'speckling' throughout the images. This improper setting may also exaggerate any regurgitation that may be present. It is therefore medically unreasonable to rely on this echocardiogram or to make any measurement or diagnosis from it." Dr. Ong concurred. Both Drs. Ong and Stern found that even with the gain, the aortic regurgitation noted was trivial and not holodiastolic.

Dr. Mancina disagreed and found the echocardiogram to be technically adequate. There is some support for his position since the gain was set at 6. He found Hymas has MAR using a JH of .33 centimeters and an LVOT of 1.83 centimeters which computes to 18%. Dr. Mancina did concede that the loop in which he measured did not demonstrate a holodiastolic jet.<sup>24</sup>

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<sup>24</sup> Dr. Mancina's testimony on this point is as follows.

Q. Doctor, referring now to -- I want -- let's start at frame 8. And I realize the reservations you say you have, but I'm going to play it from frame 8 to frame 20, which incorporates frame 10 that you utilized as a frozen to make your measurement.

MR. RAMSAY: Can you give me frame 8?

Q. All right. Doctor, as you look at the EKG, it certainly appears that we're in the beginning of electrical diastole; are we not?

A. It's very close to being -- I would have to actually see here for just a moment if we can tell electrically when diastole starts.

Q. All right. That's frame 8. Frame 9, we're certainly in diastole there; are we not?

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. There was evident speckling in the tissue even though the gain setting appears to be relatively low. Moreover, the Court finds that Wyeth has established that no reasonable medical conclusion could be drawn from this echocardiogram that Hymas has MAR. Review of the echocardiogram demonstrates that any observed jet is fleeting and not holodiastolic.

## **EE. SUSAN K. JENSEN**

Jensen relies on a September 3, 2002 echocardiogram and report by Dr. Stanley S. Schrem. Dr. Schrem found that Jensen had MAR using CAS criteria -- JH/LVOT = 24%. The sonographer found MMAR. The quality of the echocardiogram was listed as "fair."

The September 3, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Ong and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate although the gain setting apparently was at 16.<sup>25</sup>

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A. Well, it's not necessarily true, but keep moving and we'll get a better sense.

Q. Frame 10, that is the frame that you relied upon; correct?

A. That is clearly diastole.

Q. Frame 11, and it's almost gone. Frame 12, there's an argument there. Frame 13, it's gone; is it not?

A. We don't see a -- we do not see diastolic flow, but this doesn't rule out that there's aortic valve regurgitation going on in the outflow tract at this moment.

Q. It certainly doesn't confirm holodiastole; does it?

A. Not at this point, but we already saw it in three frames.

Q. All right. Next frame, and that's frame number 14. Next frame, frame number 15. Next frame, you're not seeing anything; are you? Number 16, frame 17, frame 18, frame 19, frame 20, and we're just now beginning to go into systole; are we not?

A. Well, we are -- it looks like we're at the end of diastole right at this moment.

Q. So, of the 12 to 13 frames, at most, one was able to see it in two to three frames; correct?

A. That's correct.

<sup>25</sup> Dr. Mancina conceded that some overgaining existed here.

Q. Now, Doctor, looking at this particular echo, are you suggesting to this Court that this echo is not technically-inadequate simply based on the gain with speckling all through the tissue?

A. The gain in this case is causing speckling in the tissue.

Q. And that's not acceptable according to the mandated memorandum of Dr. Mancina to his techs; is it?

Both Drs. Ong and Stern found that Jensen did not have MAR. Dr. Ong reported that:

[In the PLAX view,] [p]ages 2-4 shows color flow in the LVOT. Page 4 shows the greatest amount of AR, but it does not meet FDA positive criteria.

\* \* \* \*

[In the apical long axis view,] [t]he degree of AR in the pages with video is minute. Pages 5 and 6 showing still images with measurements revealed the calipers marks beyond the borders of the tracings.

Dr. Stern concurred, finding that “there is no holodiastolic aortic regurgitation.”<sup>26</sup>

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A. We're going to discuss that later, but the answer is that I instructed my sonographers, as all echocardiographers do, to try to go up to a level of gain and gradually bring it down to avoid speckling in the tissue, just as you described. There is speckling in the tissue. There's not a lot of speckling in the tissue. Most of the speckling is in the chamber.

Q. You don't consider that high gain, and I think there, it's a 16 according to the legend at the top left corner?

A. Well, it is 16.

Q. All right.

A. And the gain is slightly elevated.

You didn't ask the important question, which is, does that make a difference in my interpretation of the jet.

Q. I did not ask that question.

A. No, you didn't.

Q. My question to you is, even with regard to the gain of the 16 that is contrary to the mandate in your memoranda to your techs, isn't it?

A. Well, I have to say that the context of that mandate is something that we haven't discussed, but you're right. I did mandate that they use the technique of trying to eliminate speckling in the tissue.

Q. All right. Now --

A. They've done a pretty good job here. You have to do this technique yourself to understand how much better this is --

Q. Yes, sir.

A. -- than bad gain.

Q. Right.

A. This is not terrible gain. We've seen terrible gain once in a while.

<sup>26</sup> Dr. Stern's testimony in this regard is set out below.

Q. Frame 60. Anything that looks like an aortic regurgitant jet here?

A. No, because there's nothing close to the aortic valve that would pass as aortic regurgitation. You do have color, but it's not connected with --

JUDGE WALSH: You have a lot of color.

THE WITNESS: Yes, Your Honor.

Q. Frame 61. Anything?

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A. We have the same color problem here, all over the place; including in the tissue of the right ventricle.

Q. So no discernable aortic regurgitation?

A. Not to my eye.

Q. Frame 62. Anything here?

A. Again, same color, but no, I can't make AR out of this.

Q. So we've gone through five frames and we're still in diastole, right?

A. That's correct.

Q. And no aortic regurgitation?

A. That's correct.

Q. Frame 63. What about here, Doctor?

A. This may well represent aortic regurgitation, the blue area here.

Q. And let's go to Frame -- so that's one frame. Let's go to Frame 64. Is there --

A. Yes, same kind of image.

Q. Let's go to Frame 65. Anything here?

A. Again, we have three frames in a row, which would be contiguous over time and space, and they're in the right place for aortic regurgitation. They're in the right general direction.

Q. So we saw three frames out of eight so far. Let's go to the next frame. Does it appear?

A. It is no longer present.

Q. Are we still in diastole?

A. Yes, we are. This is Frame 66. We're still in diastole.

Q. Let's go to Frame 67. Anything here?

A. No, sir.

Q. Are we still in diastole?

A. Yes, we are.

Q. Frame 68?

A. This is still diastole. The mitral valve is opened. There's, virtually, no color here at all.

Q. Frame 69. Are we still in diastole?

A. Yes, we are.

Q. Any aortic regurgitation?

A. No.

Q. Frame 70?

A. We now are still in diastole because the mitral valve is opened and the QRS has not yet occurred, and now we have widespread color all over the place; probably because of atrial contraction.

Q. So we saw 12 or 13 frames of the cardiac cycle and we saw something that might have been AR in three frames?

A. I believe that's correct.

Q. And is that holodiastolic aortic regurgitation?

A. It is not, according to the FDA criteria.

\* \* \* \*

Q. Let's go to the next cardiac cycle.

A. Okay. You're still in systole because there's some mitral regurgitation. I think you need to go a little forward, T.J. That may be the beginning of diastole here. Hard to tell because there's still color flow signal back here which we don't expect in diastole.

Q. Did you want to go to Frame 12 and see?

A. In Frame 12, we have -- we are well after the T-wave, so by all rights this ought to be diastole. I can't see the mitral valve well. It's probably opened here, this color speckling. I don't see anything in the region of the left ventricular outflow tract.

Dr. Mancina disagreed. He believed that Jensen demonstrated MAR with a JH of .28 centimeters and an LVOT of 2.05 which computes to 14%. Dr. Mancina produced no evidence that the jet he attempted to measure was holodiastolic and the Court finds it was not -- it appeared at the beginning of diastole and ended shortly thereafter.

The Court finds that this was a marginal but technically adequate echocardiogram. The Court further finds that Wyeth has established that there is no holodiastolic jet which reaches MAR and no reasonable physician could conclude otherwise.

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- Q. So no AR?  
A. I do not see AR there.  
Q. Frame 13. Any AR here?  
A. We have a lot of color and it's very difficult to interpret in this sea of color. I don't see anything obvious for AR.  
Q. Frame 14. Anything here, Doctor?  
A. No, there is not.  
Q. Frame 15. Anything here, Doctor?  
A. No, sir.  
Q. 16, anything?  
A. There's a light blue color blob over here. Again, by itself, that is not enough.  
Q. And is that even high velocity?  
A. It is not in this view, no.  
Q. Frame 17. Anything here?  
A. Nothing at all.  
Q. Frame 18. Anything here?  
A. Nothing.  
Q. Frame 19. Anything here?  
A. No.  
Q. Frame 20?  
A. Nothing.  
Q. Are we still in diastole?  
A. Yes, we are. The mitral valve is open.  
Q. Frame 21. Anything here?  
A. Not at all.  
Q. Frame 22. Anything here?  
A. No.  
Q. Frame 23?  
A. Now, we have the appearance of color in many places, which probably, again, represents transport of blood from the left atrium to the left ventricle, making more color. But to get to your question, there's not convincing AR.  
Q. So in this particular cardiac cycle, we went through 12 frames and you didn't see any AR at all?  
A. That's correct.  
Q. So based on what you've seen now, is it medically reasonable to diagnose this person with medically possibly AR based on the PLAX view?  
A. It is not.

## **FF. DARLENE JEWKES**

Jewkes relies on a July 15, 2002 echocardiogram and report of Dr. John E. Lassetter. Dr. Lassetter found Jewkes had MAR using CAS criteria -- JH/LVOT = 17%.

The July 15, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Ong and Dr. Mancina. Both Drs. Ong and Stern found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Stern reported that:

The Nyquist limit was set at 46 cm/sec at the beginning of the study. Although it was increased to 51 cm/sec, this setting is only borderline acceptable. The low Nyquist settings will magnify any regurgitant jet that is present. Additionally, the color gain was set too high, creating “speckling” throughout the images. These improper settings make it medically unreasonable to rely on this echocardiogram or to make any measurement or diagnosis from it.

Dr. Ong concurred with these findings.

Dr. Mancina disagreed that the echocardiogram was not technically adequate. But his conclusion is belied by the gain setting of 16 and the evidently low Nyquist setting.<sup>27</sup>

The Court finds that Wyeth has shown that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from

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<sup>27</sup> Dr. Thomas noted that

with purported mild aortic regurgitation (17%), the Nyquist limit was set at 51 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec); furthermore, the depth could have been 10.8 cm (theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit similarly was set at 51 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec).

it. For the reasons discussed at length earlier, the high gain and low Nyquist limits make this echocardiogram unreliable.

## **GG. WINIFRED LIPPOLD**

Lippold relies on an October 14, 2002 echocardiogram and report of Dr. Edward S. Katz. Dr. Katz found Lippold had MAR using CAS criteria -- JH/LVOT = 20%. The sonographer reported a JH/LVOT = 34%. The quality of the echocardiogram was listed as "fair."

The October 14, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Ong and Dr. Mancina. All three (3) physicians reported that the echocardiogram was technically adequate though the gain setting here was 16.

Both Drs. Ong and Mancina reported that Lippold has MAR. Dr. Ong found MAR based on two (2) measurements -- 24% and 27% (the latter suggesting MMAR). Dr. Mancina found a JH of .36 centimeters and an LVOT of 1.94 centimeters, implying a JH/LVOT = 18.6%. But both physicians measured in the apical long axis view. As Dr. Ong noted,

BY MR. AGNESHWAR:

Going right to Plaintiff Lippold, I believe you said that the parasternal long axis view was available on this echocardiogram. Correct?

A. Yes, that's correct.

Q. And if you were asked to make a diagnosis based purely on the parasternal long axis view, you would agree that it would not be medically reasonable to diagnose her with FDA-positive aortic regurgitation. Right?

A. Right.<sup>28</sup>

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<sup>28</sup> By the same token, Dr. Ong indicated that from a clinical standpoint he believed Lippold has MAR.

BY MS. CARTER:

Q. The first person I'd like to talk about is Ms. Lippold, L-i-p-p-o-l-d. Can you show us page 55.

\* \* \* \*

Q. Is it your understanding from your affidavit that page 55 is the apical three view?

A. Yes.

Q. And is that one of the views that you used regurgitation?

A. Yes.

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Q. Can you see it on your screen?

A. I see something. I'm not sure if this is 55.

\* \* \* \*

Q. Can you tell us what view is being shown on this screen?

A. This appears to be a an apical tree-chamber long axis view.

Q. Do you see aortic regurgitation on this echocardiogram?

A. Yes, I do.

Q. Is this one of the views that you used to state in your affidavit that Ms. Lippold has aortic regurgitation of an FDA-positive level?

A. Yes.

Q. Can you show us page 37?

Doctor, can you tell us what is on your screen?

A. This is technically an apical five-chamber view.

Q. Did you use page 37 to confirm your diagnosis of FDA-positive for Ms. Lippold?

A. Yes.

Q. And do you see FDA-positive aortic regurgitation in this view?

A. Yes.

Q. Can you show us page 8?

Doctor, can you tell us what is --

MS. CARTER: For the record, this is page 8 of the echocardiogram.

Q. Can you tell us what is showing on your screen?

A. This is a parasternal long axis view.

Q. And you're not able to see any aortic regurgitation here, are you?

A. No.

Q. Is it your opinion that the PLAX view is nondiagnostic for Ms. Lippold?

A. It does not review a significant aortic regurgitation.

Q. But you were able to confirm that there is aortic regurgitation from the apical-three and the apical-five views. Is that right?

A. Yes.

Q. So --

JUDGE WALSH: Is there anything technically wrong with the parasternal long axis view here?

THE WITNESS: No. We see that at times because it's a two chamber -- two-dimensional image.

BY MS. CARTER:

Q. You wouldn't rely upon the PLAX view in this echocardiogram to make a diagnosis in your clinical practice, would you?

A. I would use all the views before I'd make a decision.

Q. Your affidavit says that the PLAX view is available, but you relied upon the A3 and the A5.

Is it then -- let me make sure I -- I'm confused. The PLAX view isn't available, is it? It doesn't show the aortic regurgitation.

MR. AGNESHVAR: Objection; that mischaracterizes.

JUDGE WALSH: Let's let the witness answer. Go ahead.

A. The PLAX view is available, but I did not see any aortic regurgitation.

Q. Is the PLAX view diagnostic for Ms. Lippold?

A. No, not by itself.

Q. And are you comfortable that Ms. Lippold has FDA-positive aortic regurgitation from your review of the apical three view and the apical five view of the echocardiogram?

A. Yes.

Q. And would a physician with your skill set acting reasonably conclude that Ms. Lippold had FDA-positive regurgitation even though it wasn't seen in the PLAX view?

Dr. Stern disagreed and found no sustained aortic regurgitation in the PLAX view. Moreover, he criticized Dr. Mancina for measuring the JH in a cycle which was abnormally shortened because of a cardiac arrhythmia -- a so-called "fusion cycle." Such arrhythmias have a tendency to overinflate any observed regurgitation.

Dr. Mancina compounded the problem by measuring the LVOT in the PLAX view and the JH in the apical long axis view. His worksheet indicated that his measurements were taken in the PLAX view. Dr. Mancina attempted to explain why he made the measurements he did and why they were taken from the different media locations.<sup>29</sup>

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A. Yes.

<sup>29</sup> Dr. Mancina's testimony is set out below.

Now, in Winifred Lippold, you've cited to this Court, page 53, frame 38, as the frame in which you decided to attempt to measure the jet height; correct?

A. No, it's 5538.

Q. I'm sorry, 5538. In any event, it was the apical 3 chamber view; was it not?

A. That's correct.

Q. Doctor, if you would look -- and can we look at page 7? And I'll tell you, sir, that's the PLAX view on that --

A. This is the PLAX view.

Q. Yes, sir.

And one can see where the Nyquist there is 61, and the gain, while it's a little high, it's 12. And does that PLAX view not fairly and very apparently demonstrate the structural aspects of the aortic valve and outflow tract?

A. I cannot see the aortic valve in any segment of this, so the answer to that is no.

Q. And do you see any regurgitant jet?

A. I can see the outflow tract, however.

Q. Yes, sir.

You chose not to utilize that particular view?

A. I chose not to use this view. I don't think it shows the jet.

Q. Page 4 -- page 8, another PLAX view --

JUDGE WALSH: Hold on.

MR. RAMSAY: I'm sorry, sir.

JUDGE WALSH: Do any of these loops show the aortic anulus?

THE WITNESS: It's really not well seen here, sir.

If you look, there's one flash of what I consider the valve. And if you want to go slow motion, I'll show you where I see the valve.

JUDGE WALSH: All right.

THE WITNESS: Right there. Stop. Now, in the upper segment of that outflow tract, there's valve --

Q. Right.

A. Right there. So, the anulus is going to be somewhere in this region here.

Q. Doctor, as I recall, from your testimony on Monday, there were other occasions where, in fact, you did decide to make a measurement even where, in fact, you could not definitively discern where the valves coapted; isn't that true?

A. What I'd like to see in that case is, I'd like to see the valve leaflets.

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Q. Sir, if you can answer the question I just asked.

A. Why don't you re-ask the question?

Q. On Monday, did you not, reflect in this court that in many instances, even though you could not specifically discern where the valves coapted, that, in fact, you felt it was reasonable to attempt to measure what you contended was regurgitant jet?

A. What I said at that time was that we used different frames to judge where the coaptation point is. Meaning, we like to see the valve leaflets moving. The jet may be in a different frame than the closure point of the valves or the opening part of the valves. So, we look at the structure that we see in the gray scale. And if we see the valve leaflets in, let's say, frame X, but we don't see the jet there, and, let's say, at a later point we see the jet but don't see the valve, we can still superimpose the 2D anatomy on -- on the color, just as color is superimposed on the 2D image and get a sense of where the jet is in relationship to the valve leaflets. In some cases, we don't see the valves at all.

In this case, we see one valve. We see part of it, and we see it actually near its anulus. I don't see the lower valve in any of these views unfortunately.

Q. As a practical matter on this particular PLAX, you can determine reasonably the orifice, can you not, the anulus?

A. Well, if you want me -- what do you mean by "reasonably"?

Q. Well, reasonably in order to determine whether or not there exists regurgitant jet flow.

A. I think it's a combination of looking at the information in the jet and looking at the anatomy of the anulus and valve leaflets to try to superimpose these two different points in time. In some cases, you can and in some cases, you can't.

Q. I'm going to show you --

A. I don't see the valve leaflets here except in the open position.

Q. Doctor, as you looked at page 8 in the PLAX view --

A. Yes.

Q. -- are you telling us that this view, in your judgment, was not reasonably available should you have chosen to look to see if there existed regurgitant jet?

A. I see now -- I see an area where there's a regurgitant jet, and I also see at that point a valve leaflet at the point of the regurgitant jet. So, I would feel more comfortable in this than the last one.

Q. All right. So, the PLAX was available, but you chose the apical 3 chamber view; correct?

A. Well, what you can see here is that you don't see the jet well enough. You see --

MR. RAMSAY: Move to strike.

Q. Would you answer my question?

A. I can't use this. I'm sorry.

Q. It doesn't --

A. It's not acceptable.

Q. Because you can't -- as I understand your testimony, as you reviewed it, you do not see a sustainable aortic regurgitant jet?

A. No, I do see a jet, but it's not throughout systole -- or diastole, rather.

Q. Yes, sir.

Is that the criteria that you utilize in order to make a measurement as to whether or not on color [D]oppler it lasts throughout diastole?

A. No, I have to see an adequate jet to be able to measure it. I can't an adequate jet to measure it here. And I've reviewed all other frames. So, I know there's a jet, and this doesn't represent the jet.

All said and done, the Court believes Wyeth has demonstrated that the PLAX view was available. In that view, all the experts agree that MAR is not seen. The Court has set out at length the various explanations provided by the experts as to why they took the actions they did. The Court believes that a physician acting reasonably could conclude from a clinical standpoint that Lippold has MAR. However, the test here is whether there is evidence of MAR in the PLAX view which is available so that a reasonable physician could conclude the plaintiff has MAR. The PLAX view is available here and does not support a MAR finding.

## **HH. BEVERLY LLEWELYN**

Llewelyn relies on a June 13, 2002 echocardiogram and report of Dr. Scott L. Roth. Dr. Roth found Llewelyn had MAR using CAS criteria -- JH/LVOT = 18%.

The June 13, 2002 echocardiogram was reviewed by three (3) experts: Dr. Stern, Dr. Ong and Dr. Mancina. Dr. Ong found that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. In his view, the gain was set unacceptably high. The gain setting here was 16. Drs. Stern and Mancina nevertheless found the echocardiogram to be technically acceptable.

Both Drs. Ong and Stern determined that the echocardiogram did not demonstrate MAR. According to Dr. Ong, the aortic regurgitation jet visualized in the PLAX view was “small and discontinuous.” While there was some evidence of aortic regurgitation in the apical short axis, an unapproved view, it was “a small amount.” In other instances, the origin of the jet could not be visualized. Dr. Ong measured a jet in the PLAX view at 8% with a JH of 1.5 millimeters and an LVOT of 19.5 millimeters. Dr. Stern agreed that there was only “trace” regurgitation and measured the JH/LVOT at 7%.

Dr. Mancina disagreed. According to him, Llewelyn has MAR with a JH of .41 centimeters and an LVOT of 2.01 centimeters, implying 20.4%. Dr. Mancina conceded that color flow at the low Nyquist limit of 51 was not aliased, which

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Now, I can't measure something that doesn't represent what I see in other views. This is a three-dimensional technique. You gave me two dimensions, and you gave me a fragment of the two dimensions, and you want me to measure it. I can't do it.

indicated low velocity flow. This is not characteristic of aortic regurgitation where velocities of over four (4) meters/second are to be expected.

The Court finds that Wyeth has satisfied its burden and has shown that review of this marginally acceptable echocardiogram could not support a reasonable medical conclusion that Llewelyn has MAR. The Court has reviewed the echocardiogram and finds that Drs. Ong and Stern correctly identified the aortic regurgitation as trace. No reasonable physician could conclude otherwise.

## **II. PAULETTE MADSEN**

Madsen relies on a September 18, 2002 echocardiogram and report of Dr. Raymonda Rastegar. Dr. Rastegar found Madsen had MAR using CAS criteria -- JH/LVOT = 21%. The quality of the echocardiogram was listed as “fair.”

The September 18, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Ong and Dr. Mancina. All three (3) physicians concluded that the echocardiogram was technically adequate though Dr. Chen noted that the color gain was “slightly high.”

Both Drs. Ong and Chen found that Madsen does not have MAR based on a review of this echocardiogram. Dr. Chen reported:

In real-time PLAX view images, there is a tiny AR jet that intermittently drops out of the thin proximal part of the jet just below the aortic valve. The AR jets were improperly measured by technician. The jets were not measured just below aortic valve and were measured beyond jet edges. The LVOT was undermeasured by technician. The maximal LVOT was also not selected. Even with the high color Doppler gain, the AR is trace at most.

Dr. Chen also found the jet was “too tiny and inconsistent for accurate measurement.” Dr. Ong concurred though he measured two (2) jets finding between 7% and 9%.

Dr. Mancina disagreed. In his view, Madsen has MAR but he measured her jets in the apical long axis view. His measurements of JH were .36 centimeters and

LVOT were 2.00 centimeters, yielding 18%. Dr. Mancina admitted that the PLAX view was available but he did not use it. He put it this way:

Q. Let's go to Madsen.

Now, on Madsen -- as a matter of fact, Doctor, on Madsen, in this particular case, you decided to utilize the apical 3 chamber view; correct?

A. That's correct.

Q. And yet the PLAX was available; was it not?

A. I used the three chamber view because I felt that it was representative of what I was asked to measure, and the parasternal long axis view was not.

\* \* \* \*

Q. Are you suggesting that had you measured in the PLAX view the aortic regurgitant jet, that measurement would not have yielded an FDA-positive measurement?

A. I didn't measure it here. I can't tell you for sure. I'd be happy to try to measure what I would see, but it would be superfluous because I wouldn't want to stand behind that measurement.

Q. And, Doctor, we can agree that even with the apical 3 chamber view, there's going to be some exaggeration of what everyone sees as regurgitant jet simply because the transducer now is more lateral than parallel; correct?

A. Well, we talked about -- the other day about lateral resolution versus axial resolution, but you understand that sometimes we have to measure what is available that is of good quality. So, in this case, this is of poor quality and, therefore, I would have to use the apical 3 chamber view. And I think that, in my position, you would do the same thing.

Q. Can you answer my question?

A. Lateral resolution is not a strong point of [D]oppler, and, you're right. That's a fact. I'm not trying to argue that fact.

The Court finds that Wyeth has established that this echocardiogram, when viewed in the PLAX views, does not support a reasonable judgment that Madsen has MAR. The Court finds that the PLAX view was available and should have been used. In this context, use of the apical long axis view is inappropriate.

## JJ. KIM MALDONADO

Maldonado relies on a December 6, 2002 echocardiogram and report by Dr. Marcus Brann. Dr. Brann found that Maldonado had MAR using CAS criteria --  $JH/LVOT = 24\%$ . The sonographer traced JH at .48 centimeters and the LVOT at 2.02 centimeters.

The December 6, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Ong and Dr. Mancina. Both Drs. Ong and Chen found that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. According to Dr. Chen, “[h]igh color Doppler gain settings with excessive color artifacts in static tissues and color speckles exaggerate jet size and JH/LVOT ratio. Therefore, assessment of [the] degree of aortic regurgitation using JH/LVOT can lead to overestimation and is unreliable.” Dr. Ong concurred. The gain setting on this echocardiogram was 15. Because of the technical difficulties, neither expert could further assess this echocardiogram.

Dr. Mancina disagreed. In his view, the echocardiogram was technically adequate in spite of the evident overgaining. He explained it this way:

Q. And, again, we're dealing again with a very high gain; are we not? Just look at the number in the left upper corner. It's 15.

A. I see no speckling of tissue, but it's 15.

Q. Well, based upon the 15, it is a high gain?

A. Absolutely not.

JUDGE WALSH: Let's see it in real-time.

Q. All right. Let's go to page 21 from which this was taken, I believe.

Doctor, you don't see speckling there?

A. I see speckling in the blood pool of the right ventricle. I see some blood flow in the septum, which is actually in a vessel. I see some overriding that is not speckling in the outflow tract. And I see a jet, but I don't see anything that would say this is not reasonable to read from this view.

There is not a gross amount of speckling. There's not an excessive amount of gain that prevents me from giving you a medically-reasonable judgment of that jet.

JUDGE WALSH: It looks pretty over-gained to me, Doctor.

THE WITNESS: Well, I think, sir, that you're dealing with a Nyquist of 61. You're dealing with a gain of 15 and there's not a lot of speckling of the tissue. That's all I can tell you. There's movement artifact. There is, you know, flash artifact and those kinds of things are not speckling. That's different than gain artifact.

The Court finds that Wyeth has easily established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The echocardiogram is plainly overgained. Drs. Chen and Ong have said so here. Dr. Mancina said so when he instructed his sonographers on gain settings.

#### **KK. DIXIE D. MANESS**

Maness relies on a September 9, 2002 echocardiogram and report by Dr. Paul R. Chu. Dr. Chu found Maness had MMR using CAS criteria -- RJA/LAA = 20%.

The September 9, 2002 echocardiogram was reviewed by three (3) experts: Dr. Schwartz, Dr. Sherrid and Dr. Mancina. Both Drs. Sherrid and Schwartz found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Both observed that the Nyquist limit during this study was 41 cm/sec. Dr. Sherrid notes that “[a]liasing velocity has been lowered to 41 cm/sec. This is inexplicable for strictly imaging improvement reasons. Despite this there is only trivial MR and No AR. Brief puff of early MR. CW Doppler at 212649 shows short duration of the MR.”

As Dr. Thomas noted, this unacceptable Nyquist was in no way necessary. The probe depth was 19 centimeters. The Nyquist could easily have been raised to the marginally acceptable 51 cm/sec but it was not.<sup>30</sup>

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<sup>30</sup> Dr. Thomas noted that

Dr. Mancina argues that the Nyquist limit of 41 cm/sec does not render this echocardiogram technically unacceptable. But this claim is belied by the advice given to his sonographers that a Nyquist below 51 cm/sec should *never* be used.<sup>31</sup>

The Court finds that Wyeth has easily shouldered its burden and has shown this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it.

## **LL. CAROL MANN**

Mann relies on a July 11, 2002 echocardiogram and report by Dr. Scott L. Roth. Dr. Roth found Mann had MMR using CAS criteria -- RJA/LAA - 37%. The sonographer noted that "LA (left atrium) measurements -- difficult to obtain accurate measurements. Pt (patient) has implants very low PLAX -- apical 4."

The July 11, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Both Drs. Sherrid and Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Chen noted "[c]olor Doppler gain settings are extremely high, precluding accurate assessment of degree of regurgitation by color Doppler flow mapping. Even where the gain settings are slightly less high, my best assessment would be that MR is mild at most." Dr. Sherrid concurred.

Dr. Mancina found that this echocardiogram was done in a technically adequate manner. However, his opinion is impeached by the high gain of 20, well above the maximum of 11 outlined in his memoranda.

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[for] Dixie Maness, whom I would assess as a patient most likely to require excessive depths given her 5'3" height and 290 pounds, imaging from the parasternal long-axis window utilized a Nyquist of 41 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec). In fact, the depth could have been 10.8 cm to encompass the LVOT (theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec). Moderate mitral regurgitation is claimed with an RJA/LAA of 20%, but the Nyquist limit was set at 41 cm/sec despite a depth of 19.0 cm (theoretical/Cypress maximal Nyquist limit of 52.7/51 cm/sec); furthermore, the mitral valve and left atrium could have been visualized at a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec).

<sup>31</sup> Dr. Mancina reported an LAA of 26.09 cm<sup>2</sup> which is a highly improbable number given the average LAA is 14.2 cm<sup>2</sup> ± 35D according to the Weyman Text.

Both Drs. Sherrid and Chen noted that any mitral regurgitation seen in this echocardiogram was mild at most. Dr. Chen put it this way:

[T]he color Doppler gains settings are too high to accurately assess the degree of MR on this study. In addition, the “MR” jets were measured improperly by the technician. The “MR” jets were traced beyond the jet borders. More importantly, the “MR” jets which the technician selected and measured on still frame images were recorded without corresponding real-time images. It is not acceptable to measure regurgitation on a still frame when that frame cannot be seen in its real-time context. From real-time images when color Doppler gain is slightly less high, MR is mild at most by visual assessment. In addition, the left atrial area was measured improperly. The tracing was in the left atrial cavity, not along the inner edges of the atrial wall. Maximal systolic atrial size was not selected for measurement. On the frame selected by the technician, the left atrium was imaged obliquely, the atrial was is not clearly delineated, and the true atrial size was not properly represented.

Again, Dr. Sherrid concurred.

Dr. Mancina found MMR and measured the RJA at 3.5 cm<sup>2</sup> and the LAA at 13.7 cm<sup>2</sup>, implying 25.6%.

The Court finds that Wyeth has easily established that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The overgaining dominates this echocardiogram and no reasonable physician could find otherwise.

#### **MM. LAURA L. McCOLGAN**

McColgan relies on a June 20, 2002 echocardiogram and report of Dr. Barry P. Rosenzweig. Dr. Rosenzweig found McColgan had MAR using CAS criteria -- JH/LVOT = 20%. The quality of the echocardiogram was listed as “fair.”

The June 20, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Both Drs. Sherrid and Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Chen noted that “[t]his study has high color Doppler gain with excessive color artifacts. Even so, there is no aortic regurgitation in PLAX view.” Dr. Sherrid concurred.

Dr. Mancina disagreed and argued that the gain setting was appropriate, but the gain was set at 18 which belies his conclusions. Moreover, the overgaining was compounded with a marginally acceptable 51 cm/sec Nyquist limit.

Both Drs. Sherrid and Chen examined the echocardiogram in spite of the high gains and came to the conclusion that the aortic regurgitation was trivial at most. Dr. Chen noted:

There is no aortic regurgitation in [the] PLAX view. Despite technical deficiency of high color Doppler gain, there is no aortic regurgitation visualized in real-time images of the PLAX view. The technician selected and measured 2 “AR” jets in still-frame images without corresponding real-time images. One of the “AR” jets is ill-shaped and does not have any appearance remotely like an AR jet (10:45:16). The other “AR” jet is a diamond-like color cluster and does not have a typical teardrop AR jet shape. Without corresponding real-time images to confirm, I would not consider this an AR jet. Even if this were an actual AR jet, the JH was measured improperly at the broadest part of the color cluster. The proximal part closest to the aortic valve is too tiny to measure. Therefore, there is no aortic regurgitation on PLAX view in real-time images.

Dr. Sherrid concurred and observed that the observed phenomenon was “a trivial jet that does not warrant measurement.”

Dr. Mancina again disagreed and measured a JH of .3 centimeters and an LVOT of 1.67 centimeters, implying 17.9%. But Dr. Mancina conceded that the measurement was made in systole or at the least in the transition phase.<sup>32</sup>

The Court finds that Wyeth established that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The gain was set far too high and the Nyquist was set at a marginally acceptable 51 cm/sec. Moreover, the Court finds that Wyeth has established that no reasonable physician could have based a judgment that McColgan has MAR on review of this echocardiogram.

## **NN. VICKIE NIESPOREK**

Niesporek relies on a July 17, 2002 echocardiogram and report of Dr. Robin S. Freedberg. Dr. Freedberg found that Niesporek had MAR using CAS criteria -- JH/LVOT = 17%. The quality of the echocardiogram was listed as “fair.”

The July 17, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Both Drs. Sherrid and Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Dr. Chen noted that “[t]his study has extremely high color Doppler gain settings that exaggerate jet size and make accurate assessment of the degree of regurgitation impossible.” Dr. Sherrid concurred. Neither physician attempted to measure any purported jets because of the poor technical quality of the study. Dr. Chen criticized the technique used in this study but ultimately concluded:

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<sup>32</sup> Dr. Mancina testified as follows:

Q. Doctor, as one looks at the cursor at the EKG, it demonstrates, does it not, that it is on the right side of the QRS complex?

A. It does.

Q. That would indicate systole; would it not?

A. Yes, sir.

And can you tell this Court whether it would be medically reasonable to suggest that what one sees in the outflow tract in systole was regurgitant flow and, for that matter, to measure that phenomenon?

A. No. I would say that this would be an error in the measurement. This is where I measured it.

Q. Yes, sir. That's the frame you gave to the Court.

A. Okay.

Technically inadequate study due to high color Doppler gain settings that exaggerate jet size and make assessment of regurgitation using jet dimension unreliable and inaccurate. In addition, AR jets were measured improperly by the technician. The jets were measured beyond jet edges (14:43:50, 14:44:18) or the jet was not clearly delineated (14:44:51). However, no measurements should be made on this study and no conclusions about degree of regurgitation should be made from it, due to the improper settings.

Again, Dr. Sherrid concurred.

Dr. Mancina found this to be a technically adequate study but the gain setting of 17 belies that conclusion. He also made measurements showing a JH of .26 centimeters and an LVOT of 1.9 centimeters, implying a JH/LVOT = 13.7%. As often happened in these proceedings, Dr. Mancina could not tell the cross-examiner where he took these measurements.

The Court finds that Wyeth easily satisfied its burden to show that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The gain was far too high. The Court reviewed this echocardiogram and rejects the measurements proffered by Dr. Mancina. They could not be replicated with any precision. More to the point, the poor technical quality precludes any meaningful measurement here.

## **OO. LaVERNE PENA**

Pena relies on an October 22, 2002 echocardiogram and report by Dr. Stanley S. Schrem. Dr. Schrem found that Pena had MAR using CAS criteria -- JH/LVOT = 15%. The quality of the echocardiogram was listed as “fair.”

The October 22, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. All three (3) physicians found the echocardiogram to be technically adequate.

Both Drs. Sherrid and Mancina found the Pena has MAR. Dr. Sherrid noted MAR in both the PLAX and apical 3 chamber (long) views and measured the JH/LVOT = 19% in the PLAX view. Dr. Mancina measured a JH/LVOT of 13.7%

also in the PLAX view. Dr. Mancina conceded that the valve annulus was not visible at the frame in which he measured, thereby violating the maxim that the valve structures be visible at the location in which measurements are taken. Weyman Text at 534.<sup>33</sup>

Dr. Chen disagreed. In his view, the aortic regurgitant jet was small, discontinuous and should not have been measured.

There is a tiny, non-continuous aortic regurgitant jet. The proximal part of the jet is so tiny that it drops out and cannot be measured. Therefore, AR is trace. The technician measured a color cluster that is at end-systole (14:12:07) and is not an AR jet, or measured a color void area (14:12:06).

The Court finds that Wyeth has failed to establish that no reasonable physician could conclude that Pena has MAR based on this echocardiogram. The echocardiogram is technically adequate and its review at the very least reflects a reasonable difference of opinion between qualified experts.

#### **PP. LEANN PICKETT**

Pickett relies on an April 25, 2002 echocardiogram and report of Dr. Robert M. Applebaum. Dr. Applebaum found that Pickett had MAR using CAS criteria -- JH/LVOT = 22%. The sonographer reported the technical quality as “good.”

The April 25, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Dr. Chen found the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. According to him, the “study ... [had] extremely high color Doppler gain with excessive color speckles and [a] ‘firework’ appearance in [the] real-time display of images....” Dr. Chen’s conclusion is supported by review of the gain setting on this Cypress machine which was 17. Moreover, the Nyquist was set at a marginal 51 cm/sec when it could have been set much higher based on the probe depth.

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<sup>33</sup> Weyman teaches “[t]o ensure the jet is imaged at its origin, measurements should be made only in areas where valve components are also recorded.”

Both Drs. Sherrid and Mancina found the echocardiogram to be technically adequate.<sup>34</sup> Dr. Sherrid reported a JH/LVOT = 19% and Dr. Mancina reported a JH/LVOT = 22%.

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<sup>34</sup> Dr. Sherrid acknowledged the gain was too high and he would not have set the gain this way in his laboratory.

Q. If we can look at the Pickett echo and go to Page 9, please, TJ. Dr. Sherrid would you agree with me that the color [D]oppler gain seems to be elevated on this?

A. Yes, I think the gain is a bit high.

Q. And you, actually, can see some speckling in the tissues which I think you've mentioned previously as an indication of high gain?

A. I think the gain is definitely a bit high here.

Q. And if the gain settings are high on an echo, that can exaggerate the amount of regurgitation that one might see or measure, is that true?

A. Definitely.

Q. And on this particular loop, Page 9 of the Pickett echo, the measurements done on this page could be exaggerated because of the high gain settings?

A. Yes, they definitely could be exaggerated, however it's worth noticing that I looked at Pages 9, 40 and 19, not only this frame.

Q. Sure. Why don't we go ahead and look at the other frames that you mentioned. If we can go to Page 40, TJ.

Dr. Sherrid, could you begin by telling the Court what view this is?

A. An apical long axis.

Q. And the parasternal long axis view, I think you may have already told the Court this, but it was available on this echo?

A. Yes.

Q. And let's look at your other page, Page 19. And what view is this, Doctor?

A. That's a short axis view.

JUDGE WALSH: It's a pretty colorful view, too.

THE WITNESS: Yes.

JUDGE WALSH: I mean the gain is quite evident in this particular --

THE WITNESS: Right.

Q. Let's go back to Page 40, actually, and look at the gain settings there.

Does the gain still appear to be elevated on Page 40?

A. I think the gain is a bit high.

Q. So Dr. Sherrid in light of the gain settings on this echo, would you agree with me that it would be difficult to make reliable measurements of -- quantifying aortic regurgitation with the jet height LVOT method?

A. I think this patient has mild aortic regurgitation.

JUDGE WALSH: Yeah, I think he already answered that. He said yes. In my view, the gain is high. I don't think anybody would argue with that. You see speckling in the tissue, the color box is filled. It's probably -- the jet is probably exaggerated, but all that having been said, the AI

jet, as measured by the doctor is close to 20 percent and I think you're going to have to show me something before Ms. Pickett doesn't survive the challenge. I mean the fact is that if the jet was half the size, she'd qualify, so --

\* \* \* \*

Q. Dr. Sherrid, the gain settings that we're seeing on the various pages here, are those settings the type of settings that you would permit or allow in your own echo lab?

A. No.

Q. And if one of your sonographers brought you an echocardiogram that had gain settings like this, would you discuss that issue with him or her?

The Court believes this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. However, given the multiple views by Dr. Sherrid and the testimony of Dr. Mancina, the Court finds that Wyeth has failed, but just barely, to demonstrate that the echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. There is enough, though by only a little, for a reasonable physician to conclude that Pickett has MAR.

## **QQ. ROBIN N. PLATT**

Platt relies on an October 17, 2002 echocardiogram and report of Dr. Stanley S. Schrem. Dr. Schrem found Platt had MAR using CAS criteria -- JH/LVOT = 17%. The sonographer found slightly higher JH/LVOT measurements. The quality of the echocardiogram was listed as “fair.”

The October 17, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Both Drs. Sherrid and Chen determined that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The Nyquist limit of 46 cm/sec was far too low, in the view of both.<sup>35</sup> In any event, both physicians found that any aortic regurgitation was “trivial” at most. Dr. Chen put it this way: “Nyquist velocity of 46 cm/s is too low, leading to overestimation of degree of regurgitation.

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A. I would tell them to lower the gain.

Q. And you would ask them to redo the echo to get more reliable results in order to make a diagnosis that you would want to rely on?

A. Yes, and I believe if that happened, this patient would still have mild AI.

Q. But that would be your best guess since you don't have reliable data to rely on --

JUDGE WALSH: No, it was his reasonable medical opinion.

THE WITNESS: Correct.

JUDGE WALSH: That's what it was, taking into effect the infirmities of this echo which are apparent.

<sup>35</sup> As Dr. Thomas noted that

[f]or Robin Platt, with purported mild aortic regurgitation (17%), the Nyquist limit was set at 46 cm/sec despite a depth of 13.5 cm (theoretical/Cypress maximal Nyquist limit of 74.1/74 cm/sec), and aortic regurgitation could have been imaged at 10.8 cm (theoretical/Cypress maximal Nyquist limit of 92.6/86 cm/sec). For mitral regurgitation (not claimed) the Nyquist limit similarly was set at 46 cm/sec despite a depth of 16.2 cm (theoretical/Cypress maximal Nyquist limit of 61.8/61 cm/sec).

Therefore, strictly speaking, it is technically inadequate for evaluating the degree of valvular regurgitation. However, even with the overestimation of the degree of regurgitation by low Nyquist limit velocity, there is no FDA positive regurgitation.”

Dr. Mancina disagreed. In his view, the Nyquist limit of 46 cm/sec does not harm the technical quality of the study. But as has been seen, his views about Nyquist limits are quite different when supervising his sonographers.

For the reasons repeatedly stated in this Letter Opinion, the Nyquist limit of 46 cm/sec dooms this echocardiogram as a diagnostic tool. The Court finds that Wyeth has demonstrated that echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it.

## **RR. DEBORAH POULSON**

Poulson relies on an April 25, 2002 echocardiogram and report of Dr. Robert M. Applebaum. Dr. Applebaum found Poulson had MAR using CAS criteria but gave no JH or LVOT measurements. The study quality was reported to be “fair.”

The April 25, 2002 echocardiogram was reviewed by three (3) experts: Dr. Chen, Dr. Sherrid and Dr. Mancina. Dr. Chen found that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. According to him, “[t]he combination of high color Doppler gain and relatively low Nyquist limit velocity (51 cm/s[ec]) make it impossible to reliably assess the degree of aortic regurgitation on this study.” Dr. Chen’s conclusion is supported by the gain setting on the Cypress machine which is 17 here. Both Drs. Sherrid and Mancina found that the echocardiogram was technically adequate.

Both Drs. Sherrid and Chen determined that no evidence of MAR existed on this echocardiogram. Dr. Sherrid commented that only “trivial” aortic regurgitation was found and CW showed it to be of “short duration.” Dr. Chen was more emphatic: “[E]ven with high color Doppler gain and low Nyquist velocity, there is no AR jet in the PLAX view. Furthermore, the ‘AR’ jet measured by the technician (9:54:20) is in the apical long-axis view at the end systolic - early diastolic transitional period on [the] EKG (end of T wave).”

Dr. Mancina disagreed. He found and measured a JH of .34 centimeters and an LVOT of 2.01 centimeters which implies a  $JH/LVOT = 17\%$ . Dr. Mancina argued that the aortic regurgitant jet was holodiastolic and the CW Doppler confirms this. The CW Doppler plainly shows that the jet referred to by Dr. Mancina was not holodiastolic and the Court specifically rejects his testimony on this point.

The Court finds that Wyeth has produced sufficient evidence to sustain its burden that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Moreover, the evidence demonstrates that no reasonable physician could conclude that Poulson has MAR.

## **SS. KAY RAMSEY**

Ramsey relies on an October 18, 2002 echocardiogram and report of Dr. Raymonda Rastegar. Dr. Rastegar found the Ramsey had MMR using CAS criteria --  $RJA/LAA = 29\%$ . The quality of this echocardiogram was reported to be “fair.”

The October 18, 2002 echocardiogram was reviewed by three (3) experts: Dr. Vasey, Dr. Sherrid and Dr. Mancina. Dr. Vasey concluded that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. In his view, “[t]he color flow gain was vastly excessive, rendering the color flow data uninterpretable.” Dr. Vasey’s opinion is buttressed by a gain setting of 21 which was the highest gain setting on the Cypress machine reported during this hearing. For that reason, Dr. Vasey did not even try to characterize any mitral regurgitation. In his view, it was not possible.

The Court reviewed this echocardiogram. The color box was filled with random color artifact throughout the mitral valve position of the study. Moreover, the Nyquist limit was set at the marginally acceptable range of 51 cm/sec. It could have been set much higher. As Dr. Sherrid observed, “[a]liasing velocity has been lowered to 51 cm/sec. This is inexplicable for strictly imaging improvement reasons since there has been no change in depth or any other technical reason. Despite this pages 30, 35, 54, 49 all show just mild MR.” Despite these technical concerns, Dr. Sherrid found only mild mitral regurgitation. In his view, the jets observed were neither holosystolic nor significant.

Dr. Mancina found that this echocardiogram was technically adequate though he conceded that Ramsey's echocardiogram had "a high gain." Dr. Mancina initially found Ramsey has severe mitral regurgitation ("SMR") with a RJA/LAA = 60% and reported this to the Court.<sup>36</sup> Such a finding would indicate serious pathology. After a review undertaken following his illness, Dr. Mancina concluded that Ramsey had MMR with a RJA/LAA = 29%.<sup>37</sup>

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<sup>36</sup> Dr. Mancina's Affidavit reported the following as to Ramsey.

I have reviewed the transthoracic echocardiogram of Kay Ramsey performed on October 18, 2002. The echocardiogram revealed severe mitral valve regurgitation at 60% measured in view 39 as well as the 2-chamber view. There was no aortic valve regurgitation. The left atrium was enlarged at 4.7 cm and 5.5 cm. The left ventricular ejection fraction was >60%.

<sup>37</sup> Dr. Mancina's cross-examination testimony on Ramsey is set forth in full.

Q. Let me now go to Kay Ramsey. With regard to Kay Ramsey, you've opined -- well, I have a question.

Do you recall your original Affidavit with regard to Kay Ramsey?

A. No, I don't.

Q. FTI-5187; and that's Defense Exhibit 6008.

A. This is the original you're referring to?

Q. This is the original? No, that's not it.

MR. RAMSAY: 5182, isn't that it? Yes. And if you'll blow up Ms. Ramsey -- excuse me -- the paragraph dealing with Ms. Ramsey.

MS. CARTER: She might object if we blow her up.

Q. Doctor, when you originally reviewed this echocardiogram, you reflected, and reflected under oath to this court, that it revealed severe mitral regurgitation at 60 percent, measured in view 39 as well as the 2-chamber view.

Isn't that what you told us under oath?

A. Now, tell me when you're referring to. When was it; October of 2002, I did that?

Q. No, sir.

MR. RAMSAY: What's the last day on the Affidavit? When was the Affidavit filed? Go to the last page.

Q. Sir, was this not your Affidavit?

A. Well, that's what I'm asking. Did this come out of my Affidavit --

Q. Yes, sir.

A. -- I presented to the court for this hearing?

Q. Right.

A. Okay. If that's what I said, that's what I said.

Q. All right. You said severe mitral valve regurgitation.

Then, after Monday two weeks ago, you went back with the lawyers and you re-reviewed this particular echo, and you rendered revised opinions; did you not?

A. If my revised opinion is the current opinion of 20 percent, then I did revise my opinion.

Q. Yes, sir. In fact, you reflected -- and that is --

MR. RAMSAY: I don't know if we have it as a blowup. 8054.

Q. You reflected --

The Court finds that Wyeth has satisfied its burden to show that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. Moreover, the limited review which could be performed could not support a reasonable medical conclusion that Ramsey has MMR. In so finding, the Court judges Dr. Mancina's testimony as incredible. No reasonable physician reviewing this echocardiogram could come to the conclusion that Ramsey has SMR, a very serious medical condition, with a RJA/LAA = 60% on one reading and that she has MMR with a RJA/LAA = 29% one week later.

## **TT. CHRISTINE SHAKESPEAR**

Shakespear relies on a September 17, 2002 echocardiogram and report of Dr. Edward S. Katz. Dr. Katz found that Shakespear had MAR using CAS criteria -- JH/LVOT = 18%. The quality of the echocardiogram was described as "fair."

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MR. RAMSAY: And excuse me, Judge. That's D-6009A. This is the supplementation that was rendered on April 18th through Plaintiffs' counsel. Dr. Mancina's revised opinions.

Q. You see where you even put a footnote there --

MR. RAMSAY: Give me the footnote for Dr. Ramsey.

Q. You said, Well, upon review, the earlier measurement of severe mitral regurgitation of 60 percent in fact included pulmonary venous inflow.

Isn't that what you reflected?

A. If that's what I wrote, then that's what I said.

Q. And now you come to us and you tell us that on page 35 you find that the regurgitant jet area versus the left atrial area, in your judgment, reflected FDA MR; correct?

A. Correct.

MR. RAMSAY: Let's go to page 35.

Q. First and foremost --

MR. RAMSAY: And let's just play it.

Q. Doctor, you've got a gain that, according to the legend in the top left-hand corner, is 21.

That's a very high gain; isn't it?

A. That's a high gain.

MR. RAMSAY: Give me the blow-up.

Q. And at the same time, you've got a minimal Nyquist of 51; do you not?

A. Nyquist of 51.

Q. Yes, sir. And can we agree -- I can see the sparkles even on the big screen --

A. Yes.

Q. -- you've got speckling in tissue?

A. Correct.

Q. Now -- and without being redundant, we know that this type of gain can exaggerate the size of regurgitant jet and/or create artifact as well that may be confused with a regurgitant jet; can it not?

A. We know that increasing gain can increase the jet size. We also know that Nyquist has an effect on jet size. And both of them, when they are high on the case of gain or low in the case of Nyquist, can affect jet size. That will enlarge the jet size.

The September 17, 2002 echocardiogram was reviewed by three (3) experts: Dr. Vasey, Dr. Sherrid and Dr. Mancina. Dr. Vasey found that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. “The color flow gain was vastly excessive, rendering the color flow data uninterpretable.” Nevertheless, Dr. Vasey evaluated that aortic regurgitation claim. Dr. Sherrid agreed that the gain was “too high” but also evaluated the claim. Dr. Marina disagreed that the gain was too high, even though the gain of 3 was way outside the range which he directed his sonographers to use.

Both Drs. Sherrid and Vasey found no more than “trivial AR [aortic regurgitation]” which was too insignificant to measure. Dr. Vasey noted:

Even with the high color flow gain, no aortic insufficiency is visualized. In loop 14, the purported aortic regurgitation was clearly systolic. Additionally, loop 15 is a still frame image, with no real time cine loop. In loop 46 (apical 5-chamber view), no aortic insufficiency is visualized. Finally, in continuous loop 62 in the apical view, no aortic insufficiency is visualized.

Dr. Mancina disagreed. He measured a JH of .34 centimeters and an LVOT of 1.83 centimeters, yielding a JH/LVOT of 18.6%. The Court examined the measurement technique here and finds that the alleged jet was not aliased, appeared in the last two (2) frames of diastole and plainly was not holodiastolic. The Court rejects Dr. Mancina’s testimony based on Dr. Vasey’s description of the phenomenon observed and the poor color and 2-D gain.<sup>38</sup>

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<sup>38</sup> Dr. Vasey testified on direct examination as follows.

Q. If we could go to the next plaintiff, Christine Shakespear.

JUDGE WALSH: Yes.

Q. If we could go to the qualifying echocardiogram, which is Defense Exhibit 6079. This is an aortic regurgitation claim. If we could go to page 9.

A. So now we’re in the parasternal long axis view.

JUDGE WALSH: This is another 16.2 centimeter, 51 Nyquist?

THE WITNESS: Yes.

A. And the color flow gain is high, not as high as it has been in the other two cases.

JUDGE WALSH: Looks like the 2-D gain is kind of messy, too.

THE WITNESS: Yes, it’s less penetrating than in the previous.

The Court finds that Wyeth has established that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. In any case, and for the reasons set forth in Drs. Vasey's and Sherrid's testimony, no reasonable physician could conclude that Shakespear has MAR based on a review of this echocardiogram.

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So now we're looking again for aortic insufficiency coming back from this direction. You can see a fair amount of color artifact, a jumbling, in the left ventricular outflow tract.

BY MR. WINTERS:

Q. Reviewing this on real time, is there any organized regurgitant jet shown in this loom?

A. No. An aortic insufficiency should be a repetitive holodiastolic aliased jet coming back in this direction and there just isn't one.

Q. If we could go to page 11. And if we could go frame by frame starting with frame seven.

A. You see even there just a tremendous artifact.

Q. And at what point in the cardiac cycle are we here, Doctor?

A. Now we're starting diastole, as you can see down here, and seeing no regurgitation here.

Go ahead, T.J.

Now, as you can see, that is artifact. There is no actual flow preceding from the aortic root here or the left ventricular outflow tract into the left atrium. Again, a function of the excessive color gain.

Q. If this was a reliable image, if we can just go back, would that this mean person has an aneurysm?

A. It would mean there's a shunt from the left side of the heart or the aorta down to the left atrium, which is certainly not present.

Q. Continue on.

A. So, again, no organized jet of aortic insufficiency. The aortic valve should be here so you should see something extending in this direction.

Q. I'm sorry, if we could just go back up to frame 11. What, if anything, is the mosaic color up top on this?

A. This is excessive color flow gain up here, which we've seen before. And despite that, there's no jet of aortic insufficiency.

Q. Dr. Vasey, based upon your review of this echo, would it be medically reasonable for a doctor with your training and your skill set to use this echocardiogram to diagnose Ms. Shakespear with mild aortic regurgitation?

A. No.

Q. If we can turn to

JUDGE WALSH: Could anybody actually observe a jet given -- given what is on this? I mean, is there even a suggestion of the jet?

THE WITNESS: Let's play in real time and see what could lead to that. I would say no. I don't see how you would look at that and say there's a jet of aortic insufficiency. You see something may be right here, but to me it looks like --

JUDGE WALSH: Just random color variation. It is colorful, though.

## **UU. EVA TUCKER**

Tucker relies on a July 2, 2002 echocardiogram and report by Dr. Arthur Schwartzbard. Dr. Schwartzbard found that Tucker had MAR using CAS criteria -- JH/LVOT = 15%. The echocardiogram's quality was described as "fair."

The July 2, 2002 echocardiogram was reviewed by three (3) experts: Dr. Vasey, Dr. Sherrid and Dr. Mancina. Dr. Vasey found that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. According to Dr. Vasey, "[t]he color flow gain was vastly excessive, rendering the color flow data uninterpretable. Additionally, the ultrasound penetration was poor resulting in poor quality images." Dr. Vasey's concern seems to be well founded because the gain on the Cypress machine was set at 19. The Court has examined the echocardiogram and the overgaining is evident. Moreover, the Nyquist limit was set at 51 cm/sec which is a marginally acceptable level. The Nyquist limit did not have to be set this low, in any case, because the probe depth was 16.2 centimeters. Dr. Sherrid complained about the low Nyquist but found the echocardiogram technically adequate.

Both Drs. Vasey and Sherrid found that Tucker did not have MAR. Dr. Vasey noted:

Even with the high color gain and poor ultrasound penetration, no aortic insufficiency is visualized on the echocardiogram. In real time cine loops (8, 9 and 10), there is no consistent, sustained jet of aortic insufficiency. Continuous wave Doppler (loop 34) through the LVOT shows no aortic regurgitation signal whatsoever.

Dr. Sherrid concurred. Dr. Sherrid reported no aortic regurgitation in two (2) views and trivial regurgitation in two (2) others.

Dr. Mancina disagreed. He found the echocardiogram to be technically adequate although he acknowledged the gain to be 19. Dr. Mancina claimed to measure a JH of .36 centimeters and an LVOT of 2.30 centimeters, yielding a JH/LVOT = 16%. Dr. Mancina conceded that the CW Doppler did not demonstrate any holodiastolic jets.

The Court finds that Wyeth satisfied its burden to show that this echocardiogram was not conducted in a technically adequate manner such that reliable medical conclusions regarding the presence and severity of valvular regurgitation could be drawn from it. The color gain and low Nyquist limits as well as the poor signal penetration doom this echocardiogram. Moreover, Wyeth has demonstrated that no reasonable physician could conclude that Tucker has MAR based on review of this echocardiogram.

#### IV

For the reasons set forth in this Letter Opinion, the following dispositions on Wyeth's eligibility challenges are made.

	<b>Plaintiff</b>	<b>Docket No.</b>	<b>Disposition</b>
1	Adamson, Monya A.	L-2997-04	Denied
2	Althausen, Kimberly M.	L-2343-04	Granted
3	Alvey, Judy	L-2342-04	Granted
4	Anderson, Gwendolyn	L-2340-04	Granted
5	Anderson, Marianne	L-2335-04	Granted
6	Anderson, Sheryl A.	L-3001-04	Granted
7	Anderson, Terilyn	L-3004-04	Denied
8	Andreason La Nece	L-3006-04	Granted
9	Ayen, Laura	L-2315-04	Granted
10	Beddoes, Pamela	L-3021-04	Granted
11	Benson, Laurie	L-2291-04	Granted
12	Bingham, Lynette	L-2404-04	Granted
13	Boots, Deborah	L-2427-04	Granted
14	Bowlden, Kim W.	L-3026-04	Denied
15	Bradford, Kayela J.	L-2432-04	Granted
16	Brailsford, Karen I.	L-3036-04	Granted
17	Brenchley, Ladaun G.	L-2407-04	Granted
18	Bunkall, Sylvia	L-2421-04	Granted
19	Call, Rochelle	L-2387-04	Granted
20	Chatterton, Jayne	L-2386-04	Granted
21	Conover, Erma L.	L-2385-04	Granted
22	Caulam, Carol G.	L-2462-04	Granted
23	Cowgill, Robert	L-2416-04	Granted

24	Crebs, Lisa	L-2424-04	Granted
25	Davis, Delilah	L-2460-04	Denied
26	DeWitte, Marcia	L-2475-04	Denied
27	Eyre, Danielle	L-2461-04	Granted
28	Fielding, Judy M.	L-2470-04	Granted
29	Hunsaker, Wallace J.	L-3310-04	Granted
30	Hymas, Vickie A.	L-2354-04	Granted
31	Jensen, Susan K.	L-2349-04	Granted
32	Jewkes, Darlene	L-2345-04	Granted
33	Lippold, Winifred	L-2377-04	Granted
34	Llewelyn, Beverly	L-2376-04	Granted
35	Madsen, Paulette	L-3025-04	Granted
36	Maldonado, Kim	L-3029-04	Granted
37	Maness, Dixie D.	L-3032-04	Granted
38	Mann, Carol	L-3033-04	Granted
39	McColgan, Laura L.	L-3039-04	Granted
40	Niesporek, Vickie	L-2371-04	Granted
41	Pena LaVerne	L-2319-04	Denied
42	Pickett, Leann	L-2369-04	Denied
43	Platt, Robin N.	L-2317-04	Granted
44	Poulson, Deborah	L-2314-04	Granted
45	Ramsey, Kay	L-2313-04	Granted
46	Shakespear, Christine	L-2367-04	Granted
47	Tucker, Eva	L-2367-04	Granted

An Order reflecting these dispositions is enclosed with this Letter Opinion.

Very truly yours,

  
Charles J. Walsh, J.S.C.

CJW/len  
Encl.